Treatment of
HEART DISEASE



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TO

IRIS AND WILLIAM HERBERT

PREFACE

Many years of clinical teaching, private practice and consultation work have convinced me that the general practitioner and the medical student feel a great need for a systematic and practical guide in the treatment of heart disease. This book is an attempt to provide such a guide based on my own experience in private and hospital practice.

No attempt has been made to include descriptions of additional methods favorably reported by others. It is conceded that such a plan necessarily limits the scope of the book, but it also permits greater clarity and conciseness, features which are of importance in a book of this kind.

It may be argued that the plan is somewhat dogmatic and that no single method of treatment is suitable for all patients. There is no denying that any plan of treatment may require modification because of atypical clinical features, occurrence of complications, or variations in response to therapy. Any attempt to provide suggestions for all possible contingencies would result in a mass of detail which could only prove confusing. It is my opinion that it is pedagogically more sound to familiarize the physician with the pharmacologic properties of the various drugs used in the treatment of heart disease so that he can himself institute such modifications in therapy as may be necessary. This is particularly important in determining some of the causes for failure of therapeutic response and in distinguishing untoward or toxic effects of the drugs from clinical manifestations of the disease process itself. It is for these reasons that a comprehensive survey of the pharmacologic properties of the more important drugs employed in the treatment of heart disease is included.

No attempt has been made to preface each discussion of treatment with a more or less complete summary of etiologic, symptomatic and diagnostic features of the disease to be treated, since this book is concerned primarily with therapy. It is felt that clinical descriptions of the various diseases are described adequately in the several textbooks available on heart disease. It

must be presumed that the patient has been studied carefully and that at least a tentative diagnosis has been made before the physician is ready to plan a course of treatment On the other hand I consider it profitable to devote some space to pertinent discussion of important coexisting conditions such as diabetes thyrotoxicosis pregnancy etc as they relate to the treatment of heart disease

It will be noted that a great amount of space is devoted to treatment of congestive heart failure I feel that the subject is of paramount importance since the majority of patients with almost any form of organic heart disease ultimately develop congestive heart failure It is surely no exaggeration to state that ability to treat congestive heart failure is an essential prerequisite for successful treatment of heart disease Furthermore many of the therapeutic measures employed in congestive heart failure are also useful in management of other cardiac disturbances Repetition is eliminated and space is thus conserved by referring to descriptions of such therapeutic measures in the chapter dealing with treatment of congestive heart failure

Finally I wish to acknowledge my indebtedness to Dr L N Katz for many valuable suggestions that are incorporated throughout the text Thanks are due to Dr M D Allweiss and other colleagues for additional suggestions and to Miss Paula Bennett who rendered invaluable service in preparation of the manuscript

WILLIAM A BRAMS

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THE PHARMACOLOGIC ACTION OF DRUGS USED IN THE TREATMENT OF HEART DISEASE

The suggestions in this book will prove adequate for the great majority of patients with heart disease. Variations in the clinical picture will be encountered from time to time and modifications in treatment will be necessary to meet such contingencies. The scope of this book does not permit the undertaking of detailed discussions of all possible variations in treatment. It is believed, however, that familiarity with the pharmacologic properties of the remedies employed in heart failure will aid the physician to vary his treatment sufficiently to meet all needs. It is for this reason that a comprehensive survey of current concepts regarding such pharmacologic effects is included.

DIGITALIS AND ITS ALLIES

DIGITALIS

Digitalis, long the sovereign remedy for the treatment of heart failure, was introduced into medical practice by William Withering[1] in 1785. The plant had been used for many years in the treatment of various other conditions but Withering recognized its great value in dropsy and noted many of its beneficial effects on the heart. Another century passed before its pharmacologic properties and therapeutic indications were studied adequately. Much of the best work has been done in the past twenty five years.

The standard preparations of digitalis in use today are derived from the leaves of digitalis purpurea. Many other preparations are available, including those derived from other varieties of digitalis or from sources having a digitalis like action. The effects of all these differ from standard preparations only in minor respects

none are superior and many are inferior The best clinical results are usually obtained with standard preparations of digitalis purpurea

The complete therapeutic action of digitalis is due to several glycosides the most important being digitoxin [64] The interaction of the various glycosides on one another is said to be of importance

Biological assay of preparations derived from the whole leaf is a reliable method by which quantitative activity of digitalis is determined Gravimetric estimations of various glycosides are also satisfactory

The Pharmacologic Effects of Digitalis

Digitalis applied locally, is irritant and will cause pain if injected subcutaneously or intramuscularly The major therapeutic effects are those exerted on the heart the most important being *slowing of the heart rate* and *increase in the strength of myocardial contraction* These, and other effects to be described later, are much more apparent with therapeutic doses in heart failure than in the normal heart [3, 4] Toxic manifestations with small doses of digitalis are more likely to occur if the myocardium is severely damaged This increased sensitivity of the failing heart to the beneficial and toxic effects of therapeutic doses of digitalis is of great practical importance

Increased Myocardial Contraction —The strength of myocardial contraction is increased by digitalis [2, 27, 58] the effect being more marked on the ventricles than on the auricles *Isolated* strips of myocardium, when exposed to solutions of oubain or *digitoxin* in dilutions corresponding to those occurring in man during treatment are capable of much greater force of contraction to fixed stimuli than under control conditions These experiments show that there is a direct action on the myocardium [3] Observations on the whole heart of animals and indirect studies in man support the contention that digitalis increases the strength of myocardial contraction by direct action on the muscle tissue [10, 3, 30, 60, 64, 65] Stronger myocardial contraction results in more complete emptying of the ventricles with an increase in the stroke and minute volume output of the heart [60] This improvement in pump action is augmented by slowing of the heart rate to optimum levels and by elimination of the many feeble and comparatively useless contractions of the ventricle if auricular fibrillation is

present All these factors will be discussed more fully later but the net result is reduction of venous stagnation and improvement of arterial circulation Circulation in the coronary arteries is also improved resulting in better myocardial nutrition and increased capacity for work It should be mentioned that such beneficial actions do not occur shortly after administration of digitalis unless large doses are injected intravenously, or some quickly acting preparation like strophanthin is used Hence digitalis in small dosage is no quick acting cardiac stimulant for use in emergencies

Slowing of the Heart Rate —Slowing of the heart rate by digitalis constitutes one of its major therapeutic effects Slowing is the result of two mechanisms stimulation of the vagus apparatus and direct depression of auriculoventricular conduction tissue Both mechanisms frequently play a part especially when larger doses of digitalis are employed

Stimulation of the vagus apparatus usually occurs before appreciable heart block is induced There is good evidence that the vagus endings and the carotid sinus are the chief elements responsible for vagal slowing of the heart rate rather than the vagus center as formerly believed [36] Vagus stimulation depresses the sinus node thus slowing the rate of impulse liberation from the normal cardiac pacemaker It is possible that other factors also play a part but these require further study Larger doses of digitalis depress conduction from auricles to ventricles first by way of the vagus and later by direct depression of the conducting tissues The vagal element may be eliminated by atropine but direct depression of the conducting tissue is not so influenced Hence atropine is of little value as an antidote for severe heart block induced by excessive doses of digitalis Slowing of the ventricular rate by induction of heart block is best seen in auricular fibrillation with rapid ventricular rate Here the sinus node is not operative and digitalis affects the auricular mechanism of auricular fibrillation only slightly or not at all The ventricles are slowed as a result of heart block between the auricles and ventricles so that the rate of the latter is reduced to normal or below

Slowing of the ventricular rate to optimum levels is of great therapeutic value The ventricles are 'rested since diastole is prolonged Longer diastole permits more time for venous return into the heart with consequent reduction of venous congestion

More time during diastole also permits better coronary flow with in the myocardium The passage of blood from auricles to ventricles is also facilitated by longer diastole of the ventricles The result is better nourishment of the myocardium and a more efficient heart Better filling of the heart results in a stronger myocardial contraction i e greater output into the arterial system and better nourishment of all tissues Slowing of the ventricular rate in auricular fibrillation produces such striking beneficial effects that a number of observers believed this to be the chief if not the sole therapeutic accomplishment of digitalis This conception is not entirely true since improvement has also been observed with little or no slowing of the ventricular rate particularly when the rhythm is regular [96] Slowing of the heart rate whether induced by depression of the sinus node or of the conducting tissues must not be permitted to result in a rate below norml i e below 70 to 80 beats per minute Abnormally slow rates result in very long diastole which may lead to excessive filling of the heart an effect which is undesirable when the heart is severely damaged by disease

Other Properties of Digitalis

Increase of Myocardial Excitability —Larger doses of digitalis may increase excitability of the specific conducting tissues [16] particularly of the ventricles This may result in the production of extrasystoles or paroxysmal ectopic rhythms The familiar coupling of a normal beat with an extrasystole the well known pulsus bigeminus has long been recognized as a sign of digitalis toxicity which serves as a warning that digitalis must be reduced or stopped Extrasystoles alone when not caused by digitalis should not be considered a contraindication to the use of digitalis since such irregularities may be due to poor myocardial blood supply and may disappear when coronary circulation is improved by digitalis Digitalis may induce other manifestations of increased myocardial excitability such as paroxysmal tachycardia, auricular flutter auricular fibrillation the very dangerous ventricular tachycardia or fatal ventricular fibrillation

Effects on Blood Vessels —*Blood pressure* can be elevated in experimental animals by digitalis This is due to increased cardiac output and direct constrictive action on the walls of the arteries Therapeutic doses in man do not affect blood pressure except as a

result of improved cardiac action Such a rise in blood pressure is not excessive and is an expression of improvement of the circulation In any event *neither the presence of hypertension nor the fear of inducing it should serve as a contraindication to the use of digitalis if heart failure is present*

Much attention has been paid recently to the effects of digitalis on the *coronary arteries* and in angina pectoris Strips of coronary artery immersed in solutions of digitoxin may be seen to contract [24] Experiments on animals show variable results[70] depending on the dosage used technic employed, condition of the nervous connections of the heart cardiac rate and the functional state of the heart A conspicuous change is seldom observed in the coronary arteries of the intact dog or cat, and such changes, when seen, have not been sufficiently correlated with the possible effects of the anesthetic,[30] dosage of digitalis and changes induced by the experimental technic It is difficult to compare results obtained in animal experiments under such conditions with those seen in clinical therapeutics The comparison is particularly difficult when we note that other observers failed to see unfavorable effects in experimental animals when doses were used which were comparable to those employed in clinical practice [10 3 77 85] It has been said that digitalis may induce anginal attacks in susceptible patients[40] but clinical evidence concerning this point is conflicting [41 61] Careful observations on large groups of patients with angina pectoris receiving digitalis even in large doses failed to disclose greater incidence of pain than in a similar group receiving only placebos [68] It would seem to be unwise to withhold digitalis in cardiac failure in patients who also have angina pectoris

Absorption and Fixation of Digitalis

All digitalis glycosides are absorbed from the gastro intestinal tract but not at the same rate Some are absorbed so slowly after oral administration that a considerable portion is destroyed in the gastro intestinal tract [10] Similar variability in absorption and some degree of destruction locally are believed to occur after subcutaneous or intramuscular injection [10] This if true, would make these routes much inferior to intravenous injection if parenteral administration is necessary

A so called *full therapeutic dose* of digitalis given orally, produces electrocardiographic changes in two to four hours Such changes

consist of depression of the S T segment or depression or inversion of the T wave The maximum degree of such changes is apparent in six to twenty four hours and persists for about twenty four hours, although some change may occasionally be present for as long as three weeks [6, 11, 13, 14] Such electrocardiographic changes are accepted as evidence of the onset of digitalis action on the heart but it has not yet been determined how much of these effects is due to therapeutic and how much to toxic action It is generally believed that therapeutic effects after such a full dose of digitalis occur at about the same time as the electrocardiographic changes *Small or moderate doses* of digitalis produce therapeutic effects after a longer interval three to seven days or more depending on the amount given and on the capacity of the heart to respond

It has been estimated that from 0.1 to 0.13 gm (1½ to 2 grains) of digitalis or its equivalent is used up or destroyed daily in the human body once the therapeutic effects are attained [8, 49] This is the average *maintenance dose* under these conditions but no fixed rules can be established since elimination, destruction and response to digitalis vary Elimination or destruction of a given dose of digitalis is greatest shortly after administration or when larger amounts are already present in the body [49, 4] This may explain why some patients tolerate larger maintenance doses while well digitalized and why cumulative symptoms sometimes appear when smaller doses are given over a long period of time Several instances of digitalis toxicity have come to my attention in which patients were receiving from 0.065 to 0.1 gm (1 to 1½ grains) of digitalis daily for some time The foregoing estimations of the amount of digitalis used up or destroyed daily in the body were made with digitalis which is 25 to 30 per cent less potent per unit of weight than the digitalis which is dispensed at present Hence a reduction in the average daily maintenance dose to about 65 mg (1 grain) would seem justifiable [84]

A special virtue of digitalis is its prolonged effect on the heart and the fact that addiction or tolerance is not known to occur This does not relieve the physician from the responsibility of watching the patient closely while digitalis is being given since some of the variable factors mentioned before may become operative without much warning

Severe congestion of the liver or gastro intestinal tract may

delay absorption of digitalis from the digestive tract when given orally This permits greater destruction of digitalis in the intestinal tract [30] The destroyed portion may be sufficiently great to render the remainder therapeutically inadequate The practical significance of this mechanism has been overlooked too often as shown by the fact that intravenous or rectal administration is sometimes effective when the oral route fails [6]

Intravenous injection of digitalis or its allies while not recommended for routine use, is sometimes imperative when rapid action is desirable or when the oral or rectal routes are impracticable Neither digitalis nor strophanthin is modified or fixed in the blood or lungs after intravenous injection About 10 per cent of the injected amount is fixed to the heart the remainder being taken up by the skeletal muscles liver kidneys and other tissues [30] The portion not fixed to the heart does not become available subsequently for fixation to the myocardium the one exception being the portion of digitalis which enters edema fluid or serous effusions Digitalis held by such fluid is released during diuresis and may become fixed to the heart as described later

Rectal instillation or the use of suppositories containing digitalis[56, 66] is frequently useful when the oral route is unsatisfactory and parenteral administration is not considered desirable Part of the digitalis absorbed from the rectum reaches the inferior vena cava and heart directly without encountering venous stagnation in the liver or bowel The rectal dose is the same or somewhat greater than that used orally and the entire day s requirement can be given as a single dose Absorption is fairly rapid and the results are good if a cleansing enema is given just before rectal administration

Toxic Manifestations

Toxic manifestations are due generally to overdosage or to cumulative effect after prolonged medication The cause in either case is quantitative excess in the body Toxicity may also be observed after average or small doses when the diseased myocardium is abnormally sensitive to digitalis [79]

It is generally believed that cumulation is due to gradual increment of digitalis in the heart muscle to toxic levels when the daily intake exceeds the quantity used up Large doses of digitalis or cumulative increment in the heart muscle while producing

therapeutic effects, may also cause foci of necrosis in both ventricles *chiefly the left* [75] *These effects are reversible when of* moderate degree but may remain permanent if severe This additional injury to the already diseased myocardium may make the heart muscle more sensitive to digitalis so that small doses *may now prove toxic* [76] *It is of interest to note that lethal doses* in animals caused foci of degeneration and necrosis in the brain suprarenal glands liver and kidneys as well as in the heart [80] This brings up the question whether toxic doses in man cause *similar lesions in organs other than the heart*

The *earlier* manifestations of toxicity or cumulative action are variable *No single sign or symptom always appears early* the order of appearance varies in different patients and in the same patient at different times *The more common of the earlier manifestations* of toxicity are anorexia nausea, headache, vomiting and sometimes diarrhea These and bradycardia or changes in the electrocardiogram are generally the more frequent, early signs *but there is no definite sequence and some of these manifestations may be absent* altogether It has been reported recently that general muscular weakness may be a sign of digitalis toxicity [8] It will be of interest to watch for this symptom more closely in order not to confuse it *with the muscular weakness incident to prolonged bed rest or* heart failure Attention has been directed to the fact that digitalis shortens clotting time of the blood in man and animals This may lead to thrombus formation and emboli [88, 89] Other observers could not corroborate this finding [90] It will be wise in any event not to withhold digitalis in any instance until a large and well controlled number of patients is studied to see if appreciable changes occur clinically and if emboli are actually more frequent

Vomiting is due to two mechanisms Local irritation of the gastric mucosa may cause vomiting shortly after oral ingestion of digitalis A more important and more frequent factor is reflex stimulation of the vomiting center in the brain which follows parenteral as well as oral administration [11, 19, 21] The afferent impulse reaches the vomiting center chiefly via the sympathetic nerves and to a lesser degree along the vagi The reflex arises in the heart and reaches the vomiting center in the brain along the nerve pathways mentioned *Direct application of digitalis to the region of the* vomiting center fails to induce vomiting [19] Vomiting which occurs

within an hour after oral ingestion of digitalis is probably due to local irritation of the stomach since insufficient amounts are absorbed during this time to induce toxic effects on the vomiting center [5] Vomiting when due to local irritation of the stomach can sometimes be minimized by using a different brand of digitalis or one of its allies such as digitoxin or by using rectal or parenteral administration Vomiting due to action on the vomiting center is more difficult to control unless digitalis is stopped for three or four days

Slowing of the heart rate below 65 to 70 per minute is an important sign of digitalis excess It is due to depression of the sinus node impaired conduction or both Any degree of heart block may occur the most frequent being prolongation of the P R interval A rare form of *auriculoventricular dissociation* may occur during which the auricles beat at normal rates while automatic foci in the ventricles become excited by digitalis so that they beat at a faster rate from impulses formed in them The auricles will then contract at a rate of 70 to 80 per minute while the ventricles beat at somewhat faster rates The two rhythms are independent since there is complete dissociation between the auricles and ventricles *Sino auricular* block is rare and is due to overactivity of the vagus on the sinus node *Heart block* in any form is a signal for caution in the further use of digitalis particularly if the block is caused by this drug It is sometimes necessary to persist cautiously in the use of digitalis if heart failure is still present since heart block may be due to poor myocardial circulation rather than to digitalis Digitalis in such instances is not contraindicated and may eradicate the block by improving myocardial nutrition

Digitalis intoxication may cause *arrhythmia* more rarely *tachycardia* This is due to stimulation of ectopic centers in the heart or to excessive action on its nervous connections Such toxic action on the nervous apparatus of the heart may induce or exaggerate *sinus arrhythmia* This is a sign of digitalis excess which is not heeded sufficiently in clinical practice Activation of ectopic foci in the heart by digitalis gives rise to *extrasystoles* more rarely *paroxysmal tachycardia* and occasionally to *auricular flutter* or *fibrillation* [15 42 43 44] The most frequent are ventricular extrasystoles giving rise to the well known coupling or pulsus bigeminus which consists of a normal beat followed by an extrasystole All these are important signs of digitalis toxicity but they may also be caused by

poor nutrition of the myocardium, in which case they may be abolished by digitalis There is some evidence that extrasystoles are due to disturbance in potassium balance in the myocardium when toxic doses of digitalis are at fault It was found that a single dose of 5 or 10 gm of potassium acetate as a 25 per cent aqueous solution orally could abolish extrasystoles when caused by digitalis [27] This raises the interesting question as to whether it would be useful to use potassium as described in patients who are in cardiac failure and in whom extrasystoles are present before or while employing larger doses of digitalis

Changes in the S T segment and T wave of the electrocardiogram are important signs of toxicity when induced by digitalis *The S T segment becomes depressed and the T wave lowered or inverted* in such instances [7, 8, 9, 13] Shortening of the Q T interval has been described but it is sometimes difficult to measure this interval accurately and this finding needs further corroboration [35, 8] Electrocardiographic signs of digitalis toxicity are reliable but not specific [34] They may be preceded or accompanied by other equally reliable clinical signs of digitalis toxicity [31, 3, 33, 34] Less frequent manifestations of digitalis toxicity are *mental confusion, muttering, delirium and hallucinations* It is possible that these are due to disturbed cerebral circulation or to abrupt changes in water balance in the brain such as may occur after copious diuresis [9] Delirium has been observed in arteriosclerotic patients who had been using digitalis for a long time [6] It disappears in a few days when digitalis is discontinued Other rare signs of digitalis toxicity are muscular weakness indistinct or yellowish vision and eosinophilia [16]

All effective forms of digitalis or its allies can produce toxic manifestations Preparations which are devoid of toxicity lack therapeutic power [10] But it is generally unnecessary to push these drugs to toxic levels in order to obtain satisfactory therapeutic results

PREPARATIONS AND DOSAGE OF DIGITALIS AND ITS ALLIES

The potency of digitalis per unit of weight or measure has been increased by 25 to 30 per cent in accordance with the 1936 and later editions of the U S Pharmacopeia [17] The purpose was to meet international standards

One cat unit is the approximate equivalent of 0 1 gm (1½ grains) of digitalis or 1 cc (15 minims) of the tincture although

the recent change in potency makes this comparison somewhat inaccurate The so called refined preparations and those bearing fancy names are not superior to standard preparations of digitalis and many are inferior The powdered leaves, and even the tincture may stand for years with little deterioration, provided that they are kept under ordinary storage precautions [57]

Dosage of Digitalis

The dosage of digitalis necessary in a given patient depends on several factors An attempt has been made to estimate dosage on the basis of the patient s weight The dose calculated in this manner is often too large and may prove dangerous in clinical practice A number of factors other than weight of the patient determine the dosage among which may be mentioned the rate of absorption from the gastro intestinal tract, the inherent capacity of the heart to respond with therapeutic or with toxic manifestations, the tendency of edema or serous effusions to abstract or retain digitalis thus preventing its fixation to the myocardium the presence of active infection in the myocardium the type of failure and the presence or absence of auricular fibrillation

The following working rules will be found useful and safe provided the foregoing modifying factors are kept in mind Adult patients of average height and weight who are in *moderate cardiac failure* generally require 0 1 gm (1½ grains) of the powdered leaf or 1 cc (15 minims) of the tincture by measure three to four times a day until definite improvement or signs of digitalis toxicity develop Liquid preparations must be measured, since a drop especially of an alcoholic preparation is only about 0 5 minim by measure regardless of the kind of dropper used Improvement with the foregoing dosage may be expected in four to six days but there are many exceptions since each patient poses an individual problem

Patients in *severe cardiac failure* usually require larger doses—generally 0 4 gm (6 grains) in 4 divided doses—of the powdered leaf or its equivalent during the first day A similar quantity may be necessary during the next day depending on the response The dosage is cut in half as soon as improvement becomes apparent and this dosage is continued until improvement is definite or toxic manifestations develop It is wise to start maintenance dosage when definite improvement is attained rather than to wait

for complete restoration of cardiac function, in order to avoid toxicity

Patients in *very severe cardiac failure* may be given 0 6 gm (9 grains) of powdered digitalis as an initial dose Subsequent dosage will depend on the response but 0 1 gm (1½ grains) may be given three or four times on the next day, depending on the effect Further dosage may then be regulated as in the less severe forms of cardiac failure

It should be borne in mind that the foregoing doses are for patients who have received no digitalis in the preceding week Smaller amounts should be used if the patients have been receiving digitalis although still in failure Possibly one half to three fourths of the initial dosage may be used until there is improvement or toxic manifestations develop The actual dose will have to be determined by cautious trial and by the effects on the patient The entire daily requirement can be given in one dose rectally if this route is preferable and other drugs such as sedatives may be added at the same time if required [69]

The desired therapeutic effects once they are attained, can usually be maintained by 0 065 to 0 1 gm (1 to 1½ grains) of powdered digitalis daily Maintenance doses vary with different patients and in the same patient from time to time

Massive initial digitalization based on the weight of the patient was introduced to provide quick, full digitalization in severe failure [9] Such methods may not prove safe in general practice because modifying factors are not always known in advance and the amount of digitalis already taken cannot always be estimated accurately [69] There are various formulae by which dosage can be calculated from the weight of the patient They vary from 1 to 2 minims of the tincture by measure or its equivalent per pound of body weight provided no digitalis was used before An average patient weighing 75 kg would receive about 2 gm (30 grains) of powdered leaf or 20 cc (300 minims) of the tincture in the first twenty four hours One half of the entire amount can be given at once one fourth six hours later, and the two remaining eighths at further intervals of six hours It is stated that the initial dose seldom causes toxic effects The subsequent doses can be reduced or omitted in ample time if toxicity develops since the effects of each dose become manifest in about six hours The authors of these methods recognize the limitations of such large doses and

recommend frequent graphic and clinical control, procedures hardly practicable under all conditions of clinical practice

It is generally believed that children do not respond to digitalis as well as adults This may be explained in part by the comparative rarity of auricular fibrillation in children and the frequent presence of active rheumatic myocardial infection during cardiac failure

The standard preparations of digitalis which are generally used are pills or capsules containing the *powdered leaves* and the *tincture* The powdered leaf incorporated in suppositories or the tincture diluted in 3 to 4 ounces of water may be used for rectal administration after a cleansing enema The physician will do well to become thoroughly familiar with a given brand of pill or tincture and with a suitable preparation for intravenous administration These will meet all requirements and will obviate the necessity of trying out the numerous preparations on the market none of which possesses superior qualities

A brief description of other preparations including the more common proprietary preparations will be given merely as a convenience for those who wish to try them The list is not complete and it would serve no useful purpose to enumerate all such products since many are standard preparations under different trade names The chief advantage of some is that they may be administered parenterally for rapid action while others may be tried when standard digitalis fails It will be exceptional for any of these to produce favorable results when standard digitalis fails although the more potent preparations of small volume may sometimes be better tolerated

STROPHANTHIN

Strophanthin is an efficacious drug which acts very rapidly when administered intravenously It is safe if certain precautions are observed relative to dosage and selection of proper patients It is a very good drug to use in cardiac emergencies or when oral or rectal administration of digitalis is impractical Other preparations of digitalis and its allies are also available for intravenous use in similar circumstances and the physician should familiarize himself with one of these or with strophanthin so that he may employ the drug of his choice intelligently when the need for such therapy arises

A number of years ago the author was impressed by the results obtained by Fraenkel with strophanthin and by Vaquez with oubain [81, 8] Personal use of both drugs at the bedside for a number of years and experimental study of the therapeutic and toxic properties of strophanthin K have convinced the author that strophanthin is a safe and efficient drug possessing reliable digitalis action [83] The position of comparative obscurity which strophanthin occupies in this country has prompted the author to discuss it at some length

The use of strophanthin in clinical medicine emerged from the experimental stage many years ago It has been studied carefully in a very large and ever increasing number of patients with heart failure since Fraenkel in 1906 and Vaquez in 1909 first began to use it in clinical practice Its acceptance in this country has been slow, due chiefly to the fact that some unfortunate accidents occurred because the dosage used was too large or patients were not properly selected An excellent survey of the literature and the best description of the pharmacologic action and clinical value of strophanthin may be found in the monograph of Fraenkel [8] The action of strophanthin is practically identical with that of digitalis except that strophanthin acts very much more quickly and is eliminated or used up more rapidly *Strophanthin may thus be used in cardiac emergencies where rapid digitalization with safety is necessary*

Indications for the Use of Strophanthin

Cardiac asthma acute pulmonary edema and severe abrupt heart failure are the medical emergencies which constitute the chief indications for the use of strophanthin Strophanthin will prove valuable in severe congestive failure where digitalis cannot be given orally in adequate doses as in nausea, vomiting or marked congestion of the liver and gastro intestinal tract, where absorption is slow and uncertain Strophanthin need not be continued after initial improvement has occurred or after the emergency has passed Digitalis orally in maintenance doses can be started shortly after the last injection of strophanthin

Strophanthin can be tried, but is less reliable in instances where digitalis has already failed, as in so called left heart failure with regular rhythm when due to coronary sclerosis or hypertension

Contraindications for the Use of Strophanthin

The contraindications to its use are the same as those for digitalis There is one additional precaution which must always be observed *Strophanthin must not be given to patients who are well digitalized or who have received appreciable amounts of digitalis within four or five days* Disregard of this precaution can result in abrupt additive digitalization with very serious consequences Proper dosage and observance of these precautions will prove strophanthin to be a safe rapid and efficacious digitalizing agent The question naturally arises as to whether strophanthin by its rather rapid action is likely to loosen mural thrombi with the lodgment of emboli It is the unanimous opinion of all who have extensive experience with strophanthin that it will not loosen emboli more frequently than may be expected under other conditions, including patients who receive no cardiac treatment

Dosage and Administration of Strophanthin

Three varieties of strophanthin are available Strophanthin K (Kombe) Strophanthin G (gratus) and Strophanthin H (Hispidus) The last is not used widely Strophanthin K is somewhat less toxic than oubain and about 30 per cent less toxic than ordinary strophanthin G The potency of all forms is adequate, hence strophanthin K is the drug of choice Strophanthin or oubain should be given *intravenously* only Subcutaneous and intramuscular injections are painful and absorption not very certain Rectal administration is irritating and absorption comparatively poor The digestive juices destroy strophanthin thus making oral ingestion unsuitable

The average initial dose in *severe failure* where no digitali has been used during the preceding five days is 0 5 mg An initial dose of 0 25 mg may suffice in *moderate failure* An additional injection of 0 25 mg may be given six or twelve hours after the first dose if necessary These amounts are usually adequate for the first day Maintenance doses will vary between 0 25 mg and 0 5 mg once daily if it is desired to continue with strophanthin Two to three grains of digitalis may be given by mouth for maintenance effect the first dose being administered shortly after the last injection of strophanthin Although cardiac emergencies will generally require 0 5 mg if no digitalis has been given for 5 days

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Indications for the Use of Strophanthin

Cardiac asthma, acute pulmonary edema and severe abrupt heart failure are the medical emergencies which constitute the chief indications for the use of strophanthin. Strophanthin will prove valuable in severe congestive failure where digitalis cannot be given orally in adequate doses as in nausea, vomiting or marked congestion of the liver and gastro intestinal tract where absorption is slow and uncertain. Strophanthin need not be continued after initial improvement has occurred or after the emergency has passed. Digitalis orally in maintenance doses can be started shortly after the last injection of strophanthin.

Strophanthin can be tried but is less reliable in instances where digitalis has already failed as in so called left heart failure with regular rhythm, when due to coronary sclerosis or hypertension

given where small or moderate doses of digitalis have been used shortly before it is planned to use digoxin. The average maintenance dose is 0.25 to 0.50 mg. per day. It is marketed in tablets containing 0.25 mg. The intravenous dose is 0.75 to 1 mg. diluted in 10 cc. of saline solution providing the patient has received no digitalis for several days. Intravenous injection is to be used only where very rapid action is desired or where oral medication cannot be used, as in vomiting. Oral medication is recommended for maintenance after the initial intravenous injection has taken effect. Digoxin is absorbed faster and exerts its effects quicker than standard digitalis. It is also probably excreted faster and holds a position between ordinary digitalis and strophanthin in these respects.[92]

Digilanid

Digilanid contains the lanatosides A, B and C in crystalline form. Tablets for oral use contain 0.33 mg. From 2 to 4 tablets daily are recommended for moderate digitalization and 8 to 12 tablets per day in divided doses for rapid effect if no digitalis was received for several days. The average maintenance dose is 1 or 2 tablets per day. Ampules containing 0.8 mg. in 4 cc. solution may be given intravenously in cardiac emergencies. Suppositories containing 0.5 mg. are available for rectal use. Comparative studies on the effects of ordinary digitalis and digilanid have not shown that the latter has any superior qualities.[91]

Cedilanid

Cedilanid is derived from digitalis lanata and is available in tablets containing 0.5 mg. and ampules containing 0.2 mg. per cc. of solution. Rapid digitalization may be attained by intravenous or intramuscular injection of 8 cc. Maintenance doses of one or more tablets daily are recommended.[93]

Digalen

Digalen contains cardioactive principles of digitalis. Tablets containing one half to 1 cat unit potency may be used three times daily or the solution may be given in similar dosage orally. Ampules containing 1 cat unit in 2 cc. may be given intravenously in amounts necessary to produce an effect.

0 2 mg may be given very cautiously if only average doses of digitalis were taken just before occurrence of the emergency

A dose of 0 5 mg of strophanthin is equal in potency to about 330 mg (5 grains) of digitalis Larger doses of strophanthin or repetition at shorter intervals are unnecessary and may prove dangerous It is generally wise to dilute the strophanthin in 10 or 20 cc of 10 per cent dextrose solution and to inject slowly over a period of not less than two minutes The reason for dilution and slow injection is not that the drug is dangerous It has been shown that an injected dose of strophanthin is absorbed very rapidly Dilution and slow injection exposes the heart to the drug for a longer period of time, thus permitting fixation to the heart muscle of a greater fraction of the injected dose

It has been stated that an average daily dose of strophanthin is completely destroyed or eliminated in twenty four hours so that cumulative effects are unlikely Our own observations confirm this statement [83] Hence it is safe to start digitalis orally within an hour or two after the last injection in order to maintain the beneficial effects Solutions of other necessary drugs such as mercurial diuretics or aminophyllin may be combined with strophanthin in the same syringe and injected simultaneously

Strophanthin may be compared for purposes of illustration to ordinary insulin, while digitalis is more like protamine zinc insulin Ordinary insulin is used for quick effects or where the condition of the patient changes rapidly or in emergencies Protamine zinc insulin is more useful for sustained effects when quick action is not imperative

OTHER RELATED DRUGS

Ouabain

Ouabain is now made from strophanthin G The pharmacologic action, indications contraindications dosage and method of administration are identical with those of strophanthin K

Digoxin

Digoxin is a glycoside derived from digitalis lanata and may be given orally or intravenously It may be used where ordinary digitalis is indicated and has similar effects The initial dose by mouth is 1 to 1 5 mg provided the patient has received no digitalis for the preceding week Smaller amounts, up to 1 mg may be

given where small or moderate doses of digitalis have been used shortly before it is planned to use digoxin The average maintenance dose is 0 25 to 0 50 mg per day It is marketed in tablets containing 0 25 mg The intravenous dose is 0 75 to 1 mg diluted in 10 cc of saline solution, providing the patient has received no digitalis for several days Intravenous injection is to be used only where very rapid action is desired or where oral medication cannot be used, as in vomiting Oral medication is recommended for maintenance after the initial intravenous injection has taken effect Digoxin is absorbed faster and exerts its effects quicker than standard digitalis It is also probably excreted faster and holds a position between ordinary digitalis and strophanthin in these respects [9]

Digilanid

Digilanid contains the lanatosides A B and C in crystalline form Tablets for oral use contain 0 33 mg From 2 o 4 tablets daily are recommended for moderate digitalization and 8 to 12 tablets per day in divided doses for rapid effect if no digitalis was received for several days The average maintenance dose is 1 or 2 tablets per day Ampules containing 0 8 mg in 4 cc solution may be given intravenously in cardiac emergencies Suppositories containing 0 5 mg are available for rectal use Comparative studies on the effects of ordinary digitalis and digilanid have not shown that the latter has any superior qualities [91]

Cedilanid

Cedilanid is derived from digitalis lanata and is available in tablets containing 0 5 mg and ampules containing 0 2 mg per cc of olution Rapid digitalization may be attained by intravenous or intramuscular injection of 8 cc Maintenance doses of one or more tablets daily are recommended [93]

Digalen

Digalen contains cardioactive principles of digitalis Tablets containing one half to 1 cat unit potency may be used three times daily or the solution may be given in similar dosage orally Ampules containing 1 cat unit in 2 cc may be given intravenously in amounts necessary to produce an effect

Digifolin

Digifolin is prepared from the leaves of digitalis The tablets containing 0 1 gm (1½ grains) may be given three to four times daily until the desired effects are obtained or 1 cc of the solution may be used orally in the same manner Larger doses may be used if rapid digitalization is necessary provided the patient has had no digitalis previously for several days Ampules containing 0 1 gm (1½ grains) in 2 cc can be used for intravenous injection in amounts varying from 0 2 to 0 4 gm of the drug

Digitoxin

This drug is derived from the leaves of digitalis purpurea Tablets containing 0 1 to 0 2 mg are available The average dose for full digitalization is 1 2 mg given orally An initial dose *of 0 6 mg is followed by another of the same amount in six hours* Maintenance doses of 0 1 or 0 2 mg may be given the following day Less rapid digitalization may be attained by administering 0 1 mg three times daily It is claimed that full digitalization *may be attained without irritation of the gastro intestinal tract* by oral administration The effects are otherwise the same as with standard preparations of digitalis [94, 95]

Verodigen

Verodigen has been used in doses of 0 25 mg (1 240 grain) several times daily with a maintenance dose of a similar amount once daily It is not used widely and has no advantages over other and better known preparations of digitalis

Scillaren

Scillaren is a mixture of the glycosides scillaren A and scillaren B derived from squill It produces effects on the heart similar to digitalis The effects on the heart are said to be less persistent than with digitalis but the margin of safety is narrower Tablets con taining 0 8 mg and a solution containing a similar amount per cc are available The recommended dosage for digitalization is 2 such tablets or 2 cc of the solution three to four times daily One tablet or 1 cc daily is suggested as an average maintenance dose Scillaren B for intravenous use is available in ampules con taining 0 5 mg in 1 cc for very quick action It is recommended that not more than 1 ampule be injected in twenty four hours

Urginin

Urginin is also derived from squill. Its action resembles that of digitalis. It is available in tablets containing 0.5 mg. The recommended dosage is 3 mg. a day for rapid digitalization when no digitalis has been used for a week. The maintenance dose is 0.5 mg. once daily.

THE USE OF DIGITALIS AND ITS ALLIES IN HEART DISEASE

Digitalis and its allies are useful in all forms of heart failure but the response will be modified by the type of failure and by the capacity of the heart to respond to treatment. The best results will be obtained in the earlier stages of congestive cardiac failure when recuperative power is still present. Recurrent or advanced failure leaves a residuum of permanent damage which eventually attains a level beyond reach of any therapeutic procedure. *There will be little or no benefit in heart disease not associated* with cardiac failure, in hearts which harbor active infection, and in cardiac failure due to vitamin or endocrine disturbance.

Digitalis should be administered when manifestations of cardiac failure first appear. It has been stated that moderate doses of digitalis should be used as a preventive in patients who have conditions which may lead to cardiac failure, such as hypertension, etc. Digitalis acts on the failure, not on the underlying disease, and it has already been mentioned that therapeutic doses of digitalis have only a slight effect on normal hearts as compared with those in failure. These considerations throw some doubt on the value of digitalis as a prophylactic agent while the heart still functions normally.

The most striking results are obtained in cardiac failure associated with auricular fibrillation and rapid ventricular rate. It was believed by some that success with digitalis could be obtained only in such patients because slowing of the ventricles was considered the main, if not the sole beneficial effect produced in heart failure. Dissenting reports appeared in which definite improvement was also observed in failure with regular sinus rhythm.[18, 23, 6, 38, 61, 1] Such improvement was noted with and without slowing of the heart rate. The view is now gaining ground that increase in force of myocardial contraction, due to direct action of digitalis on the myocardium, was underestimated and that ventricular slowing is only one of the favorable mechanisms induced by digitalis.

Improvement is often less striking and less frequent in cardiac failure with regular rhythm, particularly when the heart rate is not rapid. There are several reasons for this. The usual underlying causes for this form of heart failure are hypertension, coronary sclerosis or aortic valve lesions. The heart often undergoes hyper-trophy in such instances in an attempt to maintain cardiac com-pensation for as long a time as possible. Failure occurs eventually, when all myocardial reserve is exhausted, leaving little for any form of therapy to accomplish. Another possible factor is that many of these patients are well along in years with other fairly well advanced degenerative diseases and little recuperative power.

CONDITIONS WHICH INTERFERE WITH EFFICACY OF DIGITALIS

A frequent cause for failure with digitalis is *inadequate dosage*. This may be due to mistaken information relative to proper and adequate dosage in a given patient. Another possible cause is the all too prevalent idea that liquid preparations of digitalis can be dispensed in drops instead of minims by measure. A drop of aqueous or alcoholic preparation of digitalis is usually ½ minim or less by measure, regardless of the type of dropper used. Another factor is *the presence of edema fluid or serous effusions which act as a barrier to fixation of digitalis to the heart*. Much digitalis is retained in such fluid, as much as 0.46 to 0.9 cat units of digitalis activity per 100 cc. of fluid.[63] The total amount of digitalis thus retained can be very great since several liters of edema fluid must be present in the tissues before edema is manifested clinically. Digitalis, even if administered in apparently adequate dosage, will thus fail to reach the heart in sufficient amounts and cardiac failure will persist. Retention of digitalis by such fluid must be given serious attention when diuresis sets in, either as a result of favorable digitalis action or after the use of mercurial diuretics. Little digitalis is excreted in the urine, hence considerable amounts are liberated abruptly *in the blood stream during copious diuresis*. I have ob-served, as have others, that all the signs of mild or severe digitalis toxicity can appear after diuresis.[72] This is not surprising since diuresis of 3,000 cc. in twenty-four hours may abruptly liberate the equivalent of *1.5 to 2 gm. of digitalis in the blood stream*. This amount in the blood, when added to the portion already fixed to the heart, can easily produce toxic manifestations.

Active inflammation or infection in the myocardium often interferes

with the action of digitalis Such activity may be part of a generalized acute infection or may be the result of recurrent rheumatic activity in the myocardium It is important to remember that reactivation of rheumatic infection in the myocardium is a frequent cause of reappearance of heart failure in children and may interfere with the efficacy of digitalis Other forms of acute or chronic cardiac infection may result in a myocardium which is refractory to digitalis [44, 40] It is probable that the comparative inefficacy of digitalis in children is due in large part to persistent, smouldering infection or to exacerbation of active rheumatic infection in the myocardium Active infection elsewhere or the presence of high fever is said to interfere with the efficacy of all digitalis products

Digitalis is sometimes administered as a cardiac stimulant in moribund patients or to those in shock or collapse *Digitalis is not a stimulant in the sense that it acts as a cardiac whip* Cardiac efficiency is increased by digitalis without increase in expenditure of energy and without acceleration of pulse rate rise of blood pressure or drain of myocardial reserve [39]

Another cause for failure with digitalis is *inadequate absorption from the gastro intestinal tract* This may occur even with large doses given orally when passive congestion of the liver or alimentary tract exists Retarded absorption under such circumstances exposes the digitalis for a longer time to destructive action of the digestive juices Loss of digitalis in this manner may be circumvented by intravenous administration and somewhat less efficiently by rectal administration

Striking effects are rare in myocardial failure if due to *mechanical hindrances to the heart* such as constrictive pericarditis or patent ductus arteriosus Such patients show remarkable improvement when these conditions are remedied surgically The same is true in cardiac embarrassment due to *vitamin deficiency* notably Vitamin B_1, or to cardiac inefficiency due to *endocrine disturbances* such as myxedema Here too proper replacement therapy results in striking recovery after digitalis and mercurial diuretics have failed

Digitalis has *little or no effect* in tachycardia due to fever thyrotoxicosis, unstable vasomotor system shock and various toxic factors etc unless heart failure is present Paroxysmal tachycardia sometimes responds to large doses of digitalis Digitalis should always be used in such conditions if evidences of cardiac

failure begin to appear except in paroxysmal ventricular tachycardia. Auricular fibrillation with rapid ventricular rate generally responds well to digitalis, particularly in the presence of cardiac failure. The mechanism in the auricles remains uninfluenced but the resulting slowing of the ventricular rate aids greatly in improving the circulation. Persistent auricular flutter sometimes responds to full doses of digitalis as when given by the Eggleston method. Auriculoventricular block is induced and flutter of the auricles is eventually converted to fibrillation. Sinus rhythm may then set in when digitalis is discontinued at this stage but digitalis must not be stopped until auricular fibrillation has set in, regardless of the degree of auriculoventricular block induced. Digitalis is often used to eradicate extrasystoles but generally fails to do so unless the arrhythmia is due primarily to cardiac failure.

Digitalis has been used for many years in the treatment of pneumonia. It is no longer believed that death in pneumonia is due to heart failure unless serious heart disease has existed before. Toxemia and peripheral vascular collapse are now believed the chief factors, neither of which are benefited by digitalis. Careful studies on large numbers of well controlled patients have shown that digitalis does not influence the mortality rate in pneumonia.[46, 47, 48] Digitalis is indicated in pneumonia if cardiac failure begins to develop in a patient who had organic heart disease before. Its value as a prophylactic in such instances, if the heart is not in failure, still remains to be proved.

CONTRAINDICATIONS TO DIGITALIS

Heart block, especially if incomplete, is generally considered a contraindication to the use of digitalis. This is true only if block develops while a patient is receiving digitalis. Cardiac failure, if present, may still be treated cautiously with digitalis even if heart block is present.[0, 1] It is useful to see if such heart block is actually due to inherent disease, to excess digitalis, or to poor myocardial circulation. Cautious use of digitalis in the latter instance can result in disappearance of the block and in more liberal use of the drug subsequently. Partial heart block with prolongation of auriculoventricular conduction time due to inherent disease rather than digitalis intoxication may be treated in the same manner with digitalis as if the block were not present.

Bundle branch block is not a contraindication to the use of digitalis but better results are obtained by mercurial diuretics if edema or congestion is present and by the enforcement of strict bed rest [53] *Stokes Adams syndrome* if due to change from one degree of incomplete heart block to a more severe degree may be made worse by digitalis and may actually prove dangerous Complete heart block is not a contraindication to digitalis if cardiac failure is present since the degree of heart block cannot be made worse [6] [4] [5] Digitalis may actually increase the heart rate in such instances by increasing the irritability of ventricular automatic centers Improved myocardial contraction in such patients may also occur as a result of direct action of digitalis on the myocardium [74]

It has been stated that digitalis may precipitate attacks of angina pectoris in susceptible patients but subsequent experimental and clinical observations do not entirely support this view Anginal attacks do occur during the use of digitalis but their frequency is no greater than after placebos if a large series of patients is studied The frequency of anginal attacks may actually be reduced in some instances if digitalis can improve myocardial circulation adequately

Digitalis should not be used during the early stages of acute myocardial infarction unless heart failure develops Digitalis is of no value in the shock like syndrome which occurs so often in the early stages of myocardial infarction but I have observed excellent effects if *congestive myocardial failure* threatens the patient during the first few days of the attack Ectopic beats are rather easily induced in such circumstances and digitalis may aggravate the condition hence caution is advised especially in paroxysmal tachycardia [73] Rupture of the infarcted area is said to be possible if digitalis is used in the early stage of myocardial infarction but no adequate evidence has been adduced that digitalis alone was responsible Rupture of a myocardial infarct is rare and occurs when digitalis is not used Edens and others use strophanthin intravenously in angina pectoris and in acute myocardial infarction [4] Their observations were made on a large number of patients and they state that their results are very good It will be wise to suspend judgment on this point for the present I have used strophanthin during the early stages of myocardial infarction when *severe congestive failure* was present which threatened the life of the

patient Striking improvement with ultimate recovery followed in a good proportion of such instances

Extrasystoles during cardiac failure, when due to poor myocardial nutrition, may be abolished by digitalis but no such improvement occurs if the ectopic beats are due to inherent, irreversible changes in the myocardium Digitalis should not be used except with caution when such extrasystoles are a manifestation of digitalis toxicity although less importance is attached to such a sign if cardiac failure is still severe

Digitalis may prove very dangerous in ventricular tachycardia Here the automatic foci in the ventricles are hyper irritable and digitalis may exacerbate this irritability to a point where ventricular fibrillation and death may occur Quinidine in adequate doses is the drug of choice in the presence of ventricular tachycardia

There are patients who apparently cannot tolerate digitalis even in small doses Success may sometimes be attained by changing the preparation route of administration or brand of digitalis One of the allied drugs having digitalis like properties may occasionally be better tolerated than digitalis It is always well to try rectal administration under such circumstances without informing the patient that digitalis is being given Both the physician and the patient may be surprised to discover how well digitalis can be tolerated when given rectally Intolerance to digitalis is often due to extreme sensitivity to the drug because of severe myocardial damage Other remedies must then be used but the prognosis in such patients is generally very grave

DIGITALIS AS A DIAGNOSTIC AND PROGNOSTIC AID

An adequate therapeutic course of digitalis may uncover underlying but masked cardiac failure as a cause for unexplained fatigue, cough or dyspnea Similarly, the physician will look for causes other than cardiac failure when such symptoms fail to improve after adequate bed rest and digitalis

Thyrotoxicosis anemia endocrine and vitamin deficiency and pulmonary disease are some examples of other causes for symptoms which may resemble those caused by cardiac failure

The response of the patient with cardiac failure to adequate amounts of digitalis can be used as an index of prognostic value *Failure to improve generally implies a serious prognosis* The

development of toxic reactions to small doses of digitalis during treatment can also be considered a sign of grave illness with a poor prognosis [62] One must be certain however, that adequate bed rest and other suitable measures have also been employed before venturing an opinion as to prognosis in heart failure

MERCURIAL DIURETICS

The introduction of modern mercurial diuretics in the treatment of congestive heart failure was an epoch making contribution in the field of therapy Mercury in various forms had been used as a diuretic for several hundred years but its moderate diuretic effect and its toxic properties limited its usefulness Saxl and Heilig observed in 1920 that novasurol a mercurial employed in the treatment of syphilis also induced copious diuresis [98] Further clinical trial showed this mercurial to be a very reliable and potent diuretic Novasurol has since been replaced by more potent and less toxic mercurials which are now considered indispensable in the routine treatment of congestive heart failure

MECHANISM OF ACTION

It is well established that mercurial diuretics act directly on the kidneys and that the chief effect is a reduction of tubular reabsorption thus increasing the output of urine [110, 115, 1 8, 130, 135] There is some evidence that glomerular filtration is increased but these observations cannot be accepted until corroborated by further studies

Various constituents of the blood have been studied after administration of mercurial diuretics in order to determine the role played by extrarenal factors The results have been conflicting due perhaps to the fact that such studies were made at different times after the diuretic was injected No definite conclusions can be drawn from such observations until a standardized method is developed There is good clinical evidence however that extrarenal factors play a part as shown by the following observations Incisions or punctures made in the legs for mechanical drainage of edema have been observed to exude much more fluid after administration of mercurial diuretics Similar observations have been made on puncture wounds through which pleural or ascitic fluid was aspirated [114, 13]

It is possible that there is also increased loss of water from sources other than the urine, such as increased sweating since the decrease in weight after mercurial diuretics is greater than can be accounted for by the urinary output The net effect regardless of the mechanisms involved is decrease in dyspnea, improvement in nocturnal dyspnea and pulmonary edema, reduction of peripheral edema and diminution of pulmonary and hepatic congestion Pleural effusion and ascites on the other hand, do not respond so well to mercurial diuretics hence it may be necessary to remove such fluid by paracentesis if they cause discomfort Studies on venous pressure and spinal fluid pressure show that these are also markedly reduced following a favorable diuretic response [112, 1]

THE DIURETIC RESPONSE

*Diuresis begins about two or more hours after intravenous ad*ministration and somewhat later after intramuscular injection The maximum response is seen in five to eight hours and the total diuretic effect lasts about twenty to twenty four hours This is followed by a period lasting one or two days during which the urinary output is distinctly less than normal The total urinary output during diuresis will depend on several factors the more important being the degree of edema and the efficiency of the circulatory and renal systems [111]

As much as 3,000 to 4 000 cc of urine may be passed during the period of diuresis Larger amounts are not infrequent one author reporting as much as 14 500 cc in twenty four hours [100] Large amounts of chloride and base as well as water are excreted [10, 114] The output of sodium chloride may reach as much as 40 to 50 gm in one day an important factor in counteracting the tendency to edema

Mercurial diuretics are more effective if the heart is in good condition hence it will be useful to digitalize the patient with adequate doses of digitalis for about two days before mercurials are used [118] Mercurial diuretics may be combined with strophanthin in the same syringe for intravenous use in very urgent cases providing the necessary precautions are taken regarding administration of strophanthin The strophanthin will act much earlier than the mercurial and it may digitalize the patient sufficiently before the usual time necessary for onset of diuresis The day or two required for digitalization may be used to prepare the patient

with ammonium chloride in order to enhance the effect of the mercurial diuretic

Ammonium chloride is administered as enteric coated pills in doses of 2 gm (30 grains) three or four times a day during this preparatory period and for two days after injection of the mercurial [116, 135] The same cycle with ammonium chloride is repeated whenever an injection of mercurial diuretic is to be given It is stated that a *single* dose of 2 gm (30 grains) of ammonium chloride given two hours before injection of the mercurial is usually efficacious but this method has not been used widely in this country [111] Ammonium chloride alone produces little or no diuresis but when given with a mercurial diuretic it may increase the diuretic effect of the latter two or threefold The exact mechanism responsible for this effect is not clear but it is believed that some degree of acidosis is induced and that this favors release of sodium and water *from* the tissues

INDICATIONS AND CONTRAINDICATIONS

Mercurial diuretics are indicated in any form of heart failure associated with edema pleural *effusion* ascites or congestion of the lungs liver or bronchi There is good evidence that such diuretics may relieve cough due to bronchial congestion when this is a *result of* congestive heart failure Paroxysmal nocturnal dyspnea and acute pulmonary edema may be prevented even in the absence of peripheral edema or rales *in* the lungs [108, 1?9] Dyspnea on exertion or at rest if due to cardiac failure may also be relieved by such diuretics regardless of whether peripheral edema is present or not [1, 8] This is easily understood when it is remembered that vital capacity in such *patients* can be increased about 300 cc after good diuresis [12]

There are several recognized contraindications to the use of mercurial diuretics but *they* are not encountered frequently in patients with congestive heart failure Known sensitivity to mercury is a strict contraindication Mercurial diuretics *should not* be used in the active stages of glomerulonephritis or in impending uremia [134] Nephorosclerosis or albuminuria which is not due to active glomerulonephritis and the nephrotic syndrome are not considered contraindications Caution should be exercised in cachexia high fever ulcerative conditions of the bowel prostatism and gouty diathesis Urinary retention may occur in prostatism

and an acute attack of gout may be precipitated in patients with chronic or clinically dormant gout [10, 111, 1 3] It is stated that mercurial diuretics should not be used in active tuberculosis but further observations are necessary before definite conclusions can be drawn

The three preparations in use at the present time are mercupurin, salyrgan theophylline and mercuhydrin They are equally potent but mercuhydrin is less painful when injected intramuscularly

DOSAGE AND ROUTE OF ADMINISTRATION

Sensitivity to mercurial diuretics is practically never ascertained with the first injection hence a small initial trial dose is unnecessary *Mercurial diuretics should be administered early in the morning in order that most of the diuretic effect will be over by the time the patient is ready for sleep that evening The individual* dose of all mercurial diuretics is the same namely from 1 to 2 cc by intravenous or intramuscular injection The smallest, effective dose should be used in order to avoid unpleasant reactions but amounts of less than 1 cc will seldom induce satisfactory diuresis It is better to use smaller doses at more frequent intervals if necessary than larger amounts Injections may be repeated at intervals of three or more days until edema and congestion of the *lungs and liver have been relieved completely It is frequently* necessary to continue the injections perhaps at longer intervals after the patient is ambulatory in order to prevent recurrence Tolerance to mercurials does not develop and no injurious effects have been observed on the kidneys or elsewhere in the body even if used over a period of years [117, 1 4, 140]

Oral administration frequently produces unsatisfactory results and is likely to cause severe gastro intestinal disturbances Suppositories containing the same mercurials may induce satisfactory diuresis in about 50 per cent but rectal irritation is quite frequent [1] *It is stated that rectal irritation is avoided* if the same amount of mercurial is diluted in about 100 cc of water and instilled in the rectum after a cleansing enema [111]

FACTORS WHICH DECREASE THE DIURETIC RESPONSE

A good diuretic effect is not likely in moribund patients or in those whose cardiovascular or renal systems are incapable of response *The output of urine will parallel roughly the degree of*

edema hence diuresis may decrease as the degree of edema becomes less[109] Depletion of blood base chlorides or proteins may interfere but diuresis may be re established by correcting such a fault Failure with average doses of mercurial may be followed by success if larger doses as much as 4 to 5 cc are used intravenously The presence of pleural effusion or ascites sometimes prevents diuresis Removal of such collections of fluid by aspiration may be followed by satisfactory diuresis after subsequent injections of mercurials[11] It is good practice to remove such serous effusions by aspiration at the beginning of treatment since they are some what resistant to all diuretics and prolong discomfort unnecessarily It is stated that satisfactory diuresis may be obtained in edema which is resistant to therapy after some of the edema fluid is drained by incisions or punctures of the skin[131] Patients are some times encountered in whom opiates decrease the diuretic response Pituitrin sodium bicarbonate aminopyrine and sometimes pheno barbital may act in a similar manner[1 1]

UNTOWARD EFFECTS

Mercurial diuretics unlike other preparations of mercury are broken up in the body with great difficulty[130] Excretion is chiefly in the urine and elimination is rapid Elimination begins shortly after injection reaches a maximum in about an hour one half is eliminated in two hours and about 97 per cent is excreted in twenty eight hours There is thus little likelihood for the mercury as such to cause appreciable damage

Accidental deposit of mercurial diuretic in the perivenous tissues may cause painful inflammation or thrombosis Pain at the site of intramuscular injection is not rare and may last for hours Mild fever occurs occasionally, even after intravenous in jection Marked weakness thirst pains in the voluntary muscles and prostration may follow profuse diuresis This may last for a day or two but can usually be avoided by using smaller doses of the diuretic Marked fatigue restlessness and clouding of con sciousness may follow excessive loss of chlorides in profuse diuresis but these symptoms may be relieved quickly by administration of salt[119] Excessive loss of water and sodium chloride may cause severe mental symptoms including confusion and delirium Death has also been reported[99 1 6] Relief from such mental symptoms

may be obtained by administering physiologic solution of sodium chloride preferably by mouth

Auricular and ventricular tachycardia have been observed but are rare Much more serious is the development of ventricular fibrillation and sudden death [10, 11, 1 0, 131, 13, 148] This has been observed only after intravenous but not after intramuscular injection Warning symptoms sometimes occur after previous intravenous injections The more frequent signs are chills fever rash headache, vomiting urticaria pulmonary edema exfoliative dermatitis cyanosis sweating and tightness in the chest or convulsions [103, 104, 10] These and other untoward reactions necessitate a change in preparation and administration by intramuscular instead of intravenous injection

Patients may develop symptoms of digitalis toxicity if the digitalis retained in edema fluid or serous effusions is released abruptly during diuresis This complication has already been described in the chapter dealing with digitalis

The untoward reactions which may follow administration of mercurial diuretics are discussed in detail in order to familiarize the physician with them rather than to create the impression that they are frequent Untoward reactions are, in fact comparatively rare more rare than after injections of neoarsphenamine or other arsenicals used in the treatment of syphilis [106] It is the mature judgment of experienced physicians that fear of such reactions should not interfere with the use of mercurial diuretics in congestive heart failure whenever indicated provided warning signals are heeded

XANTHINES

Xanthines especially theophylline theobromine and caffeine have been used extensively in the treatment of heart disease This is due in great part to pharmacological studies which suggest that xanthines possess properties suitable for treatment of certain forms of cardiac disease

It has been demonstrated that caffeine stimulates the myocardium directly and that it may thus be considered a cardiac stimulant for use in emergencies Unfortunately these effects are of short duration and it is very likely that stimulation of psychic functions and relief of fatigue as well as stimulation of the respiratory center contribute substantially to the temporary improve

ment Theophylline and theobromine have a greater effect on the coronary arteries and on diuresis and hardly affect the cerebral cortex

The diuretic effects of xanthines are well established pharmacologically The mechanism is not clearly understood although increased glomerular filtration is said to account in part at least for the greater output of urine There is a widespread impression that they are very effective clinically but they are inferior to and less reliable than mercurial diuretics The rapid development of tolerance and cross tolerance to other xanthines as well as the likelihood of abdominal distress nausea anorexia and vomiting are further factors which limit the usefulness of xanthines as diuretics

The chief point of interest centers about the effects of xanthines on the coronary arteries There is definite evidence that xanthines dilate coronary vessels in experimental animals [1, 3] Other experiments tend to show that myocardial infarcts after ligation of a coronary artery, diminish in size after administration of xanthines [148] It is also claimed that healing of such infarcts in the experimental animal is facilitated by xanthines Other observers performing the same experiments did not obtain such results [144, 14, 149] Such contradictory reports by reliable observers have shaken the belief that xanthines play an important part in occlusive disease of the coronary arteries

Similar controversies exist in regard to the effects of xanthines in man The well controlled studies of Evans and Hoyle[147] and of Gold Kwit and Otto[143] show that the incidence of relief in angina pectoris with xanthines is no greater than with placebos This is an important observation since it is well known that angina pectoris runs an extremely variable course in any given patient Even intravenous administration produces only transient effects as shown by electrocardiographic studies [143]

It is thus obvious that the use of xanthines in occlusive or sclerotic disease of the coronary arteries is based chiefly on empiric grounds More conclusive evidence is necessary before a final appraisal can be made of the value of xanthines in man

Intravenous administration of aminophylline has been suggested in acute myocardial infarction because certain observers noted a diminution in size of the infarcts in experimental animals after aminophylline was injected Other observers noted that the

effects are of short duration while some deny that such changes take place The value of xanthines in such instances therefore rests on controversial evidence Nor can one say that oral administration of xanthines produces beneficial effects which could not be better explained by bed rest and other measures employed routinely in such patients It is a fact, however, that intravenous administration of 0 48 gm of aminophylline may occasionally relieve pain in the early stages of myocardial infarction, even when morphine fails

The Cheyne Stokes type of respiration and paroxysmal nocturnal dyspnea may be sufficiently disturbing at night to prevent sleep and thus hinder the natural recuperative powers of the patient Theophylline ethylenediamine (aminophylline) frequently relieves such disturbing breathing when due to cardiac failure [14] [146] [150] [151] Relief may be obtained in a few minutes and lasts for six to eight hours after an intravenous injection of 0 48 gm given very slowly to prevent unpleasant side effects The aminophylline may be combined with a mercurial diuretic in the same syringe in an attempt to prevent subsequent attacks Cheyne Stokes respirations and paroxysmal nocturnal dyspnea may often be prevented by an intravenous injection of 0 24 to 0 48 gm of aminophylline before bedtime Rectal administration before bedtime of the same amount in the form of a suppository or solution in about 100 cc of water after a cleansing enema is also effective but not as dependable as intravenous injection Oral administration is generally ineffective even if similar doses are used Intramuscular administration causes considerable pain at the site of injection

UNFAVORABLE REACTIONS

A cup of coffee or tea contains from 0 1 to 0 2 gm (1½ to 3 grains) of caffeine Excessive use of these or other preparations of caffeine may cause restlessness excitement insomnia palpitation, muscle tremor and tachycardia Anorexia nausea vomiting and epigastric distress may be caused by oral use of caffeine or other xanthines Intravenous administration of aminophylline may cause flushing thoracic oppression, nausea and vomiting Sudden death has been reported in a few instances after injection but these are quite rare [15]

INDICATIONS FOR THE USE OF XANTHINES

The chief indications for the use of xanthines are congestive heart failure with edema, and in diseases of the coronary arteries The diuretic effect is of value in relief of congestion of the lungs and liver and aids in eradication of edema It has been pointed out that this can be accomplished more quickly and more thoroughly with mercurial diuretics

Xanthines have been employed in diseases of the coronary arteries for more than half a century [141] The employment of xanthines in angina pectoris coronary sclerosis and in the later stages of coronary thrombosis has become traditional all over the world in spite of the fact that there is no really reliable experimental or clinical evidence to justify their use The physician who wishes to continue this ritual should at least choose a preparation which is not likely to induce gastro intestinal upsets Theobromine calcium salicylate in doses of 0 5 gm after meals three times daily or enteric coated tablets of 0 1 gm of aminophylline will usually answer such requirements

QUINIDINE

The beneficial effects of quinine in auricular fibrillation were first observed by one of Wenckebach s patients who noted that his attacks of paroxysmal auricular fibrillation could be terminated by taking 1 gm of quinine [154] A few years later Frey showed that quinidine one of the alkaloids of cinchona bark was much more potent than quinine in auricular fibrillation [161] Further studies revealed that quinidine was about five to ten times as potent as quinine and that the former could restore normal rhythm in from 50 to 65 per cent of selected patients with auricular fibrillation [165 166 175 1 8 183]

MECHANISM OF ACTION

Quinidine is an effective but dangerous drug It depresses nearly all myocardial functions the most important clinical effect being lengthening of the refractory period Slowing of conduction in the auricles and ventricles and from the former to the latter as well as depression of the vagi are also of clinical significance [1 6]

The circus theory of Lewis postulates that a wave moves rapidly in a more or less circular pathway in the auricles and that this circulating wave gives rise to the oscillations of auricular fibrilla

tion and flutter. The circulating wave is not a complete ring but has a gap between its head and tail. All the tissue occupied by the circulating wave and a portion of the gap at the tail of the wave are in a refractory phase. The tissue at the remainder of the gap remains responsive to further stimuli. Quinidine prolongs the refractory phase or depresses this responsive segment of the gap so that an obstacle to stimuli is formed in a larger portion of the path of the circulating wave. The circulating wave not finding any responsive tissue in which to move is thus extinguished. The sinus node is then enabled to take over its function as pacemaker of the heart with restoration of normal rhythm.[169, 184]

Electrocardiographic studies of auricular fibrillation during administration of quinidine disclose gradual slowing of auricular oscillations after which normal rhythm may be re-established in the auricles quite abruptly. Auricular fibrillation is usually associated with an auricular rate of 450 to 500 or more per minute but poor conduction permits only a relatively small proportion of the auricular contractions to reach the ventricles. Slowing of the auricular rate to about 200 or 250 per minute permits improvement of auriculo-ventricular conduction with the possibility that a greater number of auricular beats can now reach the ventricles. This mechanism and depression of the vagi by quinidine may explain the increased ventricular rate which is sometimes encountered during quinidine therapy before normal rhythm is restored.[1, 184] Auricular fibrillation is sometimes converted to auricular flutter during quinidine therapy before normal rhythm is restored. The slower auricular oscillations of auricular flutter and depression of the vagi may give rise to a significant increase in ventricular rate as described.[16]

Quinidine can produce changes in the electrocardiogram. The T wave may be flattened and the duration of PR, QRS, and of QT may be lengthened.[177, 16] Quinidine may produce cardiac standstill by severe depression of the sinus node and all other specific muscle tissue in the heart, even after normal rhythm is restored.[160, 18] Ventricular fibrillation has been observed in rare instances and this as well as cardiac arrest may be the cause of sudden death for which emboli or other anatomical causes cannot be found.

It has been stated that coronary flow can be increased by quinidine as a result of dilatation of the coronary vessels.[1, 0] This

and restoration of normal rhythm may provide better circulation within the myocardium This observation if corroborated should lead to more frequent use of quinidine in arrhythmia due to coronary artery disease

TOXIC REACTIONS AND UNTOWARD EFFECTS

Quinidine is a valuable remedy in cardiac arrhythmia but its toxic effects are sometimes unpredictable Death has been reported with as little as 0 2 gm (3 grains) but this is very unusual [163] Sudden death occurred in one of my patients several days after quinidine had restored normal rhythm The patient was not in cardiac failure and felt well a moment before death Others have reported similar deaths without apparent cause either clinically or at autopsy [177] It is possible that abrupt ventricular fibrillation or cardiac standstill was precipitated by quinidine in these patients

Quinidine may produce various toxic manifestations These include palpitation vertigo diarrhea urticaria eczema fever syncope convulsions, nausea vomiting epigastric distress headache tinnitus collapse and respiratory failure [155, 157, 173] It is generally wise to discontinue quinidine when any of these occur although Lewis considered faintness, diarrhea abdominal pain and headache as relatively unimportant while a rise in ventricular rate palpitation or ventricular extrasystoles were considered very dangerous and called for immediate discontinuance of the drug [1]

It is stated that serious manifestations of toxicity are not frequent unless there is a history of sensitivity to quinine The difficulty lies in the fact that patients may not have had occasion to use quinine before It will be wise to withhold quinidine unless a test dose shows no sensitivity and to select patients in whom there are good prospects of success with little or no apparent danger

Quinidine may produce electrocardiographic changes These have been described under mechanism of action Such electrocardiographic changes when produced by quinidine suggest caution in the further use of the drug Intraventricular block when due to causes other than the quinidine does not constitute a contraindication to the use of this drug [167]

A history of embolism or the possibility that mural thrombi may become detached from the walls of dilated auricles when normal rhythm is restored has long been considered a contra

indication to the use of quinidine There are a number of authors, however, who do not believe that the incidence of emboli is any greater in patients who receive quinidine than in those who do not [1, 1, 1, 7, 183, 18] There are reports of patients in whom emboli no longer occurred after the use of quinidine [171, 186] One may therefore use quinidine in cardiac arrhythmia with recurrent embolization if the situation is desperate and other measures fail

ABSORPTION AND EXCRETION

Quinidine is absorbed rapidly from the gastro intestinal tract and is eliminated chiefly by the kidneys [163] Solubility is not an important factor since all forms of quinidine are converted to quinidine hydrochloride in the stomach and are thus absorbed at about the same rate [175] It would be of interest to know if a similar *conversion occurs when no hydrochloric acid is formed* in the stomach

A single oral dose will cause slowing of the auricular rate in about thirty minutes with a maximum effect in two or three hours This maximum effect is maintained for about thirty minutes after which there is a gradual decline with return to the previous auricular activity in twenty four hours [175, 178] The maximum concentration in the blood following a single oral dose can be observed as early as thirty minutes and none may be found in the blood after an hour The maximum concentration in the heart muscle after a single oral dose occurs in about sixty minutes and disappears completely in about seven hours [1, 9] A good con centration may be found in the blood plasma in an hour or less after a single oral dose with a maximum rise in two to four hours [18] A single intravenous injection will cause maximum slowing of the auricles in about ten minutes and this effect will last about fifteen minutes with gradual return to the previous rate in about one to five hours [157, 181] It is obvious that quinidine is best administered orally every hour and certainly at intervals not greater than two hours if it is desired to build up a level in the body which is to be of therapeutic value

DOSAGE AND ROUTES OF ADMINISTRATION

A test dose of 0 2 gm (3 grains) of quinidine sulfate should be given to uncover possible sensitivity to the drug [1, 2] Early mani festations of sensitivity to quinidine include nausea vomiting

headache, tinnitus, deafness, urticaria and tachycardia. Quinidine is best discontinued if these or other toxic manifestations occur.[161] It is usually recommended that a test dose be given one day before quinidine therapy is instituted. This seems like a waste of time since maximum effects after oral administration may be expected in about two hours or less. It seems more logical to proceed with quinidine therapy if no untoward effects are noted one or two hours after the test dose is given.

Various methods have been suggested for administration of quinidine. A useful method consists of administration of 0.2 gm. (3 grains) of quinidine sulfate orally and to repeat the same dose after an hour if no untoward symptoms have developed. No harm will be done if untoward symptoms develop after such small doses and sufficient time will have elapsed for maximum effects to develop. No time is lost since quinidine may be continued in doses of 0.2 gm. (3 grains) every hour until normal rhythm is restored, toxic symptoms develop or a maximum of 2 gm. (30 grains) is given that day. This method permits gradual increment of quinidine in the body until a point is reached at which the drug becomes effective. The same method may be repeated daily or larger doses may be used every hour in very resistant cases. It has been observed that although larger doses are more likely to restore normal rhythm than smaller amounts, the effects are not proportional to the actual increase in dosage.[178] As much as 0.6 to 0.8 gm. (9 to 12 grains) has been administered per dose in resistant cases but it is seldom necessary or wise to exceed 2.4 or 2.76 gm. (36 to 40 grains) in any single day.[160, 173, 185] Attempts to restore normal rhythm with quinidine may be made daily for as long as a week but quinidine should be discontinued if it has not proved successful after such a period.[160] Restoration of normal rhythm may be maintained by administration of 0.2 gm. (3 grains) or more every four hours day and night for two or three days after which it may be reduced to four times daily for a week. The number of doses per day may then be reduced gradually in accordance with the needs of the patient. Larger maintenance doses are often required if larger amounts of quinidine were necessary to restore normal rhythm.[18]

Other routes of administration may be attempted in great emergencies or when the oral route is impractical because of vomiting or difficulty in swallowing. Intramuscular injection is

followed by rapid absorption and produces quick effects It is said not to cause more toxic manifestations than oral administration The solution is prepared by adding quinidine hydrochloride 15 gm, antipyrene 15 gm and urea 20 gm to 100 cc of distilled water The solution is sterilized by passage through a Berkefeld filter after which it may be stored in sterile ampules or bottles for future use [158] No local reactions are reported The solution consists of 0 15 gm of quinidine for each cubic centimeter of fluid The average initial dose is 0 45 to 0 6 gm Favorable effects may be expected in one and one half to two and one half hours after which the same dose may be repeated at intervals of two hours until normal rhythm is restored Larger amounts may be injected if the foregoing doses prove unsatisfactory

Intravenous administration has been employed in ventricular tachycardia and other urgent or very resistant cases A solution containing 3 3 gm (50 grains) of quinidine sulfate in 500 cc of normal saline or 5 per cent dextrose solution is permitted to flow into the vein at a rate of about 100 cc per hour [180] Good results have been reported but it is generally held that intravenous injection of quinidine is dangerous and the results have been disappointing in our patients Intravenous administration of quinine dihydrochloride is safer and may be used when the intravenous route is necessary A solution of 0 25 gm ($3\frac{3}{4}$ grains) of quinine dihydrochloride is available in ampules which should be diluted in 20 cc of sterile water and this may be injected very slowly almost drop by drop until normal rhythm is restored or a total of not more than 0 5 gm ($7\frac{1}{2}$ grains) is injected

Maintenance doses of quinidine should be given orally as described after normal rhythm has been restored by any method of administration

INDICATIONS

The chief indication for quinidine is *recent or paroxysmal auricular fibrillation* in otherwise healthy hearts The best results are obtained if there is little or no organic heart disease or cardiac failure [166, 1, 1, 3, 183] Auricular fibrillation which is of more than three or four months duration or which is associated with cardiac failure is much more resistant to quinidine therapy and normal rhythm if restored will frequently revert to auricular fibrillation after a short period of time

It may be advisable in some instances to restore normal rhythm in seriously damaged but otherwise compensated hearts since auricular fibrillation with rapid ventricular rate may precipitate cardiac failure. The use of quinidine in such instances may postpone cardiac failure by eradicating auricular fibrillation and slowing the ventricular rate to normal.[183] It is questionable, however, if it is wise to attempt restoration of normal rhythm with quinidine if the ventricular rate is within the normal range. The results are less favorable if cardiac failure is due chiefly to serious organic heart disease rather than to the auricular fibrillation. Restoration of normal rhythm will prove disappointing in such patients since it does not remove the chief factor in the production of the cardiac failure.[164, 168] Such patients frequently have a return of auricular fibrillation after a short period of time. Hence it is generally better to digitalize such patients in order to slow the ventricular rate to 75 or 85 per minute as well as to improve cardiac failure as much as possible.

Quinidine is a myocardial depressant; hence it is always wise to restore cardiac compensation by digitalis and other measures if cardiac failure is present before attempting the use of quinidine.[16, 164, 16, 166, 17, 1, 3, 175, 183, 18] Digitalis, even in full doses, does not interfere with the action of quinidine; hence there need be no hesitancy in its use in such circumstances.

There are rare occasions when digitalis, bed rest and other measures fail to improve cardiac failure as long as auricular fibrillation persists. There are also very rare instances where emboli occur at frequent intervals while auricular fibrillation is present. Quinidine has sometimes restored normal rhythm in such patients with cessation of further embolization and improvement of the cardiac status.[1, 9, 186] Administration of quinidine in such instances is admittedly a dangerous procedure but such a step may prove justifiable if other measures fail.

Auricular fibrillation which is due to thyrotoxicosis is very resistant to quinidine and often disappears spontaneously after thyroidectomy. Auricular fibrillation and other ectopic rhythms which persist for two weeks or longer after thyroidectomy may frequently be abolished by quinidine.[173]

Auricular flutter and paroxysmal tachycardia, including ventricular tachycardia, are frequently influenced favorably by quinidine. The same precautions should be used in the presence of

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that administration of concentrations of about 100 per cent should not be continued for more than forty eight hours

Dyspnea which occurs in the course of congestive heart failure or in acute myocardial infarction is probably the most frequent indication for oxygen therapy The diffusion of oxygen from the inspired air to the capillaries of the lung in these conditions is rendered difficult for the following reasons Engorgement of the blood vessels in the alveolar walls results in edema and thickening of these walls Fibrotic changes which occur later may act as further barriers to the diffusion of oxygen from the alveolar spaces to the vessels of the altered alveolar walls Reduction of space within the alveoli adds further difficulties The reduction in alveolar capacity is due to dilatation of blood vessels within the alveolar walls thickening of the septa and to transudation of fluid within the alveolar spaces To these are added reduction of normal pulmonary excursion when the lungs become more rigid from pulmonary engorgement All of these factors reduce vital capacity and favor the development of dyspnea and anoxemia [189]

Other mechanisms including pulmonary reflexes chemical changes in the blood and slowing of the circulation may play a more important part in paroxysmal dyspnea but there is no unanimity of opinion about these mechanisms All these factors cannot be overcome by oxygen therapy but benefit may be expected where the diffusion of oxygen can be increased across the barriers in the alveolar walls and spaces by increasing the partial pressure of oxygen in the inspired air

Cyanosis when due to the inadequate oxygenation of the blood within the lungs may also be relieved by oxygen therapy [189, 190, 191] Additional mechanisms such as dilatation of the venules of the skin and mucous membranes also play a part but such mechanisms will hardly respond directly to oxygen therapy Hence dyspnea and cyanosis need not be relieved to the same degree or at the same time by oxygen therapy

Acute pulmonary edema when due to heart failure may respond dramatically to administration of oxygen under positive pressure [193] Concentrations of 100 per cent or less may be used with this method A special mask such as the meter mask may be used in order to regulate the degree of positive pressure This form of oxygen therapy is described under discussion of methods of administration

cardiac failure as were outlined in the discussion of the use of quinidine in auricular fibrillation Quinidine often fails to abolish extrasystoles and is quite ineffective in sinus tachycardia [1, 6] Quinidine is used frequently in the first two or three weeks after acute myocardial infarction to prevent serious cardiac arrhythmia It use in such instances is based on observations made on animal experiments A large and well controlled series of clinical observations is necessary before the actual value of such measures can be determined

PRECAUTIONS

Patients receiving quinidine should be at bed rest until they are ready for maintenance doses It has already been mentioned that patients in cardiac failure should be digitalized until cardiac compensation is restored and the ventricular rate slowed before quinidine therapy is begun Reversion to auricular fibrillation or flutter a short time after quinidine is discontinued is usually evidence that quinidine will probably fail to keep the patient in normal rhythm It is probably best in such instances to slow the ventricular rate as much as possible with digitalis and to maintain this effect with adequate maintenance doses of digitalis It is generally inadvisable to use quinidine in chronic auricular fibrillation in auricular fibrillation with a normal ventricular rate in old or feeble patients in very large hearts with dilated auricles in severe coronary disease, serious cardiac failure and when the ventricular rate cannot be slowed by digitalis [160, 163, 166]

OXYGEN

Oxygen is an important *therapeutic measure in the treatment* of heart disease The greatest benefit will be obtained when heart disease results in conditions which interfere with normal oxygen exchange within the lungs It is important however that oxygen be furnished in adequate concentrations continuously until digitalis diuretics and bed rest can exert their maximum effects on the heart and circulation

INDICATIONS

Oxygen therapy to be of value should be employed early in the course of treatment before irreversible changes occur No deleterious effects have been encountered although it is stated

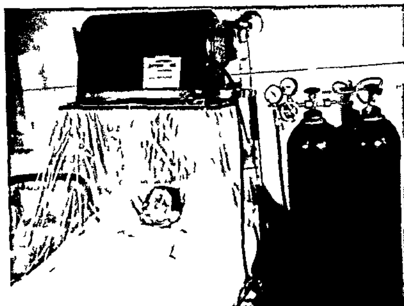


Fig 1 — A typical arrangement for administration of oxygen by a tent. Note the warning notice against open fire or flame.

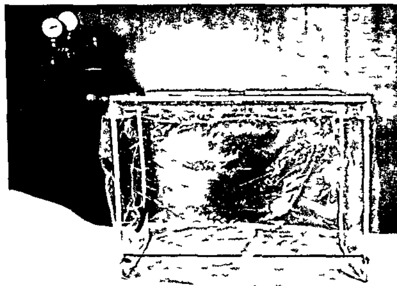


Fig 2 —Box arrangement for administration of oxygen to infants. Note the open top and the hose near bottom from which oxygen escapes within the box.

Passive congestion of the lungs, pulmonary infarction or bronchopneumonia may interfere sufficiently with gas exchange in the lungs to induce or aggravate dyspnea, cyanosis or general discomfort. Oxygen administered by tent or nasal catheter, often provides relief in such instances although concentrations of 100 per cent may be required in very severe cases.

Paroxysmal dyspnea and periodic breathing, when the result of cardiac failure, are relieved or may be prevented by continuous oxygen therapy. Cheyne Stokes breathing may disturb the patient during sleep but this form of periodic breathing can usually be relieved immediately by inhalation of 100 per cent oxygen. Lower concentrations of oxygen may also be beneficial but relief will be much more gradual.

Severe or persistent pain when due to coronary disease such as status anginosus or myocardial infarction may respond to oxygen therapy even if morphine and other measures fail.[139, 193, 194] It will generally be necessary to use concentrations of 100 per cent with a special mask such as the BLB mask as described under methods of administration. Lower concentrations of oxygen such as 40 or 50 per cent are seldom efficacious in the relief of such pain.

Oxygen therapy may also relieve disturbing cough when caused by congestive heart failure.[194] Restlessness, which is not infrequent in myocardial infarction or in cardiac failure may respond favorably to oxygen therapy.

METHODS OF ADMINISTRATION

It is wasteful and useless to administer oxygen by a funnel held over the nose and mouth. Oxygen therapy to be useful should provide *a continuous flow of oxygen in adequate concentration until no longer needed*.

The description of the methods of administration which follow are taken largely from the excellent monograph by Barach.[193]

Administration by Oxygen Tent

This is the method employed most frequently in routine oxygen therapy. It can provide concentrations of oxygen of about 50 per cent and has the additional advantage that temperature and relative humidity within the tent can be regulated in accordance with the needs of the patient. A temperature of about 70 F and a relative humidity of 40 to 60 per cent within the tent will gene

blood into the lungs This permits rapid disappearance of pulmonary edema with relief of breathing

The mask is applied so that the patient at first exhales against a positive pressure of 1 or 2 cm of water for about fifteen minutes The positive pressure is increased by 1 cm every fifteen minutes until 3 or 4 cm are attained This is maintained until all signs of pulmonary edema have disappeared after which the pressure is lowered by 1 cm every two or three hours until the patient feels comfortable without positive pressure The mask must be

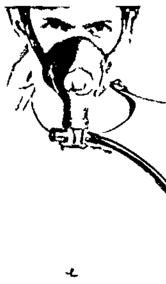


FIG 3

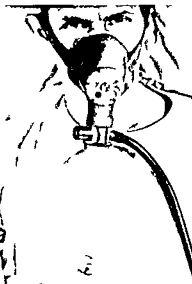


FIG 4

Fig 3 —Face mask for administration of very high concentrations of oxygen
Fig 4 —Face mask for administration of oxygen under pressure Note orifices on mask for regulation of positive pressures varying from zero to 4 cm of water

reapplied as in the beginning of treatment if evidences of pulmonary edema recur at any time Oxygen concentrations of 100 per cent are employed frequently although lower concentrations may be used A flow of 12 to 15 liters per minute may be required when the mask is first applied but the flow is reduced later so that the bag partially collapses at the height of inspiration

High concentrations of oxygen or oxygen under positive pressure are maintained only as long as necessary The patient should then be placed in an oxygen tent as described for one or more weeks Oxygen therapy should not be terminated abruptly even

ually prove comfortable but these should be *regulated in accordance* with the requirements of the patient

A different arrangement may be used for infants or small children where greater access to the patient is necessary A so called open box tent is used which consists of transparent sides but no top The inflow of oxygen is near the base of one of the sides so that the oxygen remains at the lower levels of the box and at the level of the patient s nose and mouth A flow of about 6 to 7 liters per minute will furnish oxygen concentrations of about 50 per cent at the lower levels within the open box

Administration by Nasal Catheter

This method is described on page 68

Administration of High Concentrations of Oxygen

A special mask is necessary when concentrations of about 90 to 100 per cent are desired The BLB (Boothby Lovelace and Bulbulian) mask which encloses the nose and mouth is satisfactory The mask is attached to a small bag and the flow of oxygen is so *adjusted that the bag collapses at the end of inspiration but not* completely A flow of 6 to 8 liters per minute from the oxygen source is usually sufficient although some patients may require more Concentrations of 100 per cent may be administered safely for as long as forty eight hours and probably longer, after which the patient should be placed in a tent where he may continue to receive concentrations of about 50 per cent

Administration of Oxygen under Positive Pressure

The Meter mask as described by Barach is equipped with a metal disc which contains five orifices of varying diameters [103] Each orifice controls a different degree of positive pressure against which the patient exhales when the mask is applied No pressure is exerted when the largest orifice is used but the remaining orifices are employed when pressures of 1 2 3 or 4 cm of water are desired Administration of oxygen under positive pressure is very useful in treatment of pulmonary edema Positive pressure is applied against the walls of the alveoli during expiration by this method This counteracts the tendency to transudation from the vessels in the walls of the alveoli into the alveolar spaces The pressure also compresses the vessels in the walls of the alveoli thus reducing pulmonary engorgement by interfering with inflow of

or sleep induced The sensations of hunger fatigue and other forms of discomfort are also relieved or abolished thus inducing restfulness which is followed by sleep lasting from six to eight hours

Sensitivity of the respiratory system is reduced so that breathing becomes slower dyspnea is reduced and disturbing Cheyne Stokes respirations are relieved, provided the dose of morphine is not too great The cough reflex is allayed and bronchial secretions are reduced but cough due to passive congestion of the lungs or bronchi is remarkably resistant to opiates or other sedatives

Indications

The indications for the use of opiates in heart disease are the induction of sleep or rest when it is believed that other remedies are not sufficiently powerful to accomplish such results Morphine or its allies in average doses i e 16 mg (1/4 grain) are very useful in acute pulmonary edema of cardiac origin Smaller doses the equivalent of 8 to 10 mg (1/8 to 1/6 grain) of morphine can alleviate or even prevent paroxysmal nocturnal dyspnea or disturbing Cheyne Stokes respiration In all of the foregoing conditions the best results will be obtained if morphine or its allies are administered by subcutaneous injection

Untoward Effects

Itching is frequent after any opiate including codeine The secretion of urine is not diminished but retention may occur from powerful spasm of the bladder sphincter [19] The urine may contain reducing substances and actual hyperglycemia and glycosuria may occur after larger doses of morphine [196 197] This is of importance in treating diabetics with heart disease or in cases of acute myocardial infarction where transient glycosuria may occur or the diabetic state may be made worse Nausea and vomiting are fairly frequent and may prove troublesome These are due to a central effect on the brain and may occur several hours or the day after administration Some patients develop headache excitement disturbing dreams or rapid review of thoughts which may keep the patient awake

The lethal dose of morphine is said to be about 0 2 gm (3 grains) or more but myxedematous patients are very sensitive to opiates I know of a myxedematous patient who died after the

if oxygen is administered by tent or nasal catheter The concentration of oxygen may be reduced to 40 per cent if dyspnea and other signs of cardiac disturbance have disappeared This is maintained for about two days after which the concentration is reduced to 35 per cent for another two or three days provided there is no discomfort Oxygen therapy may then be discontinued completely if the patient continues to be comfortable

A word of caution is necessary in regard to mental symptoms which may develop during oxygen therapy in patients with severe anoxia and cyanosis Such patients may occasionally develop headache or become irrational lethargic or stuporous due to sudden change in oxygen tension in the brain induced by oxygen therapy This may persist for several days but oxygen therapy should not be changed or discontinued since all these symptoms will disappear and the patient will then show remarkable improvement in his mental condition

HYPNOTICS AND SEDATIVES

Adequate sleep and rest are essential in the treatment of cardiac failure The choice of a hypnotic or sedative will depend on the cause of sleeplessness or restlessness Morphine or one of its allies will be indicated if pain or dyspnea is the cause of restlessness or loss of sleep while barbiturates bromides or similar sedatives will usually suffice if nervous or emotional factors are at fault

OPIATES

Morphine or its allies when injected subcutaneously are prompt and dependable sedatives and hypnotics There is an old and unwarranted belief that opiates are dangerous in heart disease This misconception is probably based on the observation that morphine fails to rescue moribund patients Extensive clinical experience has shown that opiates are safe in all forms of heart failure with the possible exception of cases in which there is deep cyanosis or where the respiratory center shows evidences of marked depression

Mechanism of Action

Morphine acts chiefly on the higher cerebral centers decreasing sensitivity of the cerebral cortex to pain and other stimuli [19, 195] This effect occurs quickly even before the sensorium is affected

are obtained. The physical condition and mental state of the patient may be the deciding factor in the production of unpleasant reactions.

Barbiturates are absorbed rapidly from the stomach and induce sedation or sleep in one or two hours. Unpleasant aftereffects, the so-called hangover symptoms, are not rare. Undesirable effects are more likely to occur in older patients, emotionally unstable persons or in patients with cerebral arteriosclerosis.[108] Hangover symptoms consist of headache, lassitude, confusion, visual disturbances, ataxia and emotional instability. These may persist for several hours after awakening but are seldom serious. Such manifestations may be due to excessive dosage, slow elimination or personality traits which predispose the patient to untoward responses to barbiturates. Smaller dosage or choice of a shorter acting barbiturate may prevent such symptoms if personality traits of the patient are not at fault. All barbiturates are capable of producing such reactions if given in sufficient dosage.

Other more disturbing reactions consist of skin eruptions, alarming dreams, cerebral excitement, delirium, vertigo, ataxia and headache. Less frequent are agranulocytosis, generalized pains, hyperglycemia, itching and fever.

Chronic barbiturate intoxication may result from prolonged use, poor elimination or slow disintegration in the body. The symptoms consist of apathy, thick speech, ataxia, nystagmus, squint, failing memory and palsies in various regions of the body.[101]

Excretion of barbiturates is chiefly via the urine and is slow. A single large dose may require as much as ten days for complete elimination and much longer if the patient's renal function is impaired. It will be wise to interrupt administration of barbiturates after a week or ten days in order to avoid cumulative symptoms. Cumulative symptoms, once they appear, may persist for two or three weeks after the last dose has been taken.

Habituation is possible but is more in the nature of a psychological need for the drug, such as occurs with alcohol, rather than with morphine.[90, 91] There are no genuine withdrawal symptoms with physical suffering such as occur in opium addiction.

Indications and Dosage

Barbiturates may be used in restlessness or insomnia when due to nervous or psychic factors. The comparatively insignificant

second injection of 16 mg of morphine which was given for severe renal colic

Dosage and Methods of Administration

Oral or rectal administration of opiates is too slow and too uncertain in action for routine use in cardiac disease Subcutaneous injection is the method of choice and is followed by effects in ten to fifteen minutes Intravenous administration may be used when immediate relief of very severe pain is desired

Opiates are excreted by the mucous membrane of the gastro intestinal tract regardless of the original route of administration The excreted opiates are reabsorbed and again exert their action although in a lesser degree

The preparations usually employed are morphine dilaudid pantopon and codeine Demerol in doses of 50 to 100 mg subcutaneously or intramuscularly can relieve pain but not as well as morphine Subcutaneous injection of 16 mg (¼ grain) of morphine, 20 mg (1/3 grain) of pantopon or 3 mg (1/20 grain) of dilaudid are of equal value in the relief of pain or acute pulmonary edema although here too morphine will be found most dependable The usual amount of morphine used for intravenous injection is 16 mg (¼ grain) dissolved in 2 cc of sterile distilled water The injection should be made very slowly, drop by drop, until the desired effect is obtained or the full dose is given Pounding sensation in the head dizziness and other unpleasant reactions may be experienced if the injection is made too rapidly but these pass off in a few minutes

Codeine sulfate in doses of 16 to 32 mg (¼ to ½ grain) orally is used to allay the cough reflex Codeine phosphate in doses of 32 mg (½ grain) may be injected subcutaneously for the same purpose Codeine is far less effective than morphine or related substances for relief of pain Untoward effects are itching constipation cyanosis and depression of the respiratory center with slow or Cheyne Stokes breathing

BARBITURATES

Barbiturates are used widely as sedatives or hypnotics They act chiefly on the thalamus and brain stem in contrast to bromides which act on the cerebral cortex The size of the dose and the rate of elimination determine whether sedative or hypnotic effects

are discontinued and elimination is accelerated by oral administration of sodium chloride

Less serious are the after effects which may occur after average individual doses of bromides These consist of headache mental dullness or confusion which may persist for several hours

Bromides are reliable sedatives and are not habit forming They are useful in treating excitable patients provided care is taken not to induce chronic bromism by continued administration This may be prevented by discontinuing bromides after several days and using another sedative for an equal period of time if necessary

The average dose of almost any bromide is 1 gm (15 grains) two or three times daily preferably after meals The effervescent tablet contains about this amount of bromide and is pleasant to take The elixir of triple bromides contains a similar amount of bromide in a teaspoonful and is a useful preparation in liquid form

CHLORAL HYDRATE

Chloral hydrate is a safe sedative and hypnotic which has no injurious effect on the heart Studies on patients receiving fairly large doses of chloral revealed no clinical or electrocardiographic evidence of injury to the heart even when chloral was continued for as long as ten days

Doses of 1 to 2 gm (15 to 30 grains) induce drowsiness which progresses to sleep in about an hour Chloral hydrate being very soluble is easily absorbed when taken orally or given rectally It is excreted in a changed form in the urine with occasional production of reducing substances which may be mistaken for glycosuria Sleep is induced by depression of the sensory functions of the brain and lasts from five to eight hours This may be followed at times by temporary headache or confusion Chloral has no analgesic properties hence it may prove ineffective if pain or dyspnea cause restlessness or lack of sleep

Rectal administration is preferable since chloral has an unpleasant taste It is generally given in doses of 0 65 to 1 3 gm (10 to 20 grains) combined with about twice this amount of bromides and dissolved in about 5 or 6 ounces of water This is best administered after a cleansing enema Addiction after prolonged use is known but is very rare

analgesic effects greatly reduce the usefulness of barbiturates where pain severe dyspnea or other strong stimuli cause restlessness or interfere with sleep

Phenobarbital is the preparation most frequently used and its properties are representative of the entire group Sedation can usually be attained by oral administration of 16 to 32 mg (¼ to ½ grain) several times a day A dose of 0 065 to 0 130 gm (1 to 2 grains) is the average to induce sleep The sodium salt in somewhat larger doses can be injected subcutaneously to induce sleep if the oral route is impracticable Seconal and nembutal are shorter acting barbiturates and are less likely to leave after effects when given in doses of 0 1 gm (1½ grains) to induce sleep All barbit urates may be given rectally as suppositories in about twice the amount necessary for oral use Barbiturates are safe in cardiac disease when used in average therapeutic doses since such amounts produce no injurious effects on the heart or kidneys [201, 202]

Prolonged use of any barbiturate results in a form of tolerance which necessitates the employment of larger amounts to produce the same effects A cross tolerance to all other barbiturates also develops in time so that is will be advisable to discontinue bar biturates after a period of a week or ten days

BROMIDES

Bromides reduce abnormal excitability of the brain but they do not have the sleep compelling power of opiates barbiturates chloral or paraldehyde Bromides are effective in producing a state of calm in an otherwise excitable or restless patient but they often fail if pain dyspnea or other form of discomfort is responsible for the restlessness Sleep may be facilitated by calming the pa tient but bromides cannot be considered true hypnotics

Absorption is rapid when administered orally but elimination is slow hence cumulation is possible Bromide intoxication from cumulation is not at all rare and is often unrecognized even by experienced clinicians The chief manifestations are acne or pus tular skin eruptions apathy mental dullness poor memory de fective speech tremor ataxia psychic depression psychoses and low grade fever *Serious psychic changes are possible when the* concentrations of bromides in the blood reach levels above 150 mg in 100 cc These manifestations disappear when bromides

THE TREATMENT OF CONGESTIVE HEART FAILURE

Congestive heart failure may be defined as inability of the heart to pump adequate blood into the arterial system with resulting engorgement in the greater or lesser venous circuits The clinical manifestations of congestive heart failure will be determined by predominance of congestion in either the greater or lesser venous circuit Predominant congestion in the greater venous circulation will be manifested by engorgement of the liver and peripheral veins edema and by cyanosis Other manifestations also occur but they are not distinctive Predominant congestion of the lesser venous circuit produces engorgement of the lungs with respiratory distress such as paroxysmal dyspnea acute pulmonary edema wheezing respirations at night cough which is refractory to ordinary treatment and persistent rales at the bases of the lungs Both the greater and lesser venous circuits are usually involved in congestive heart failure but there will generally be sufficient predominance of engorgement in one or the other circuit to justify such a clinical distinction

The aim of treatment in congestive heart failure will be to improve cardiac function as much as possible and to reduce the activities of the patient to bounds within the capacity of his heart It will seldom be possible to restore anatomical integrity of the heart and it will be equally difficult in most instances to eradicate the underlying causative disease responsible for functional or structural changes in the heart Notable exceptions are surgical obliteration of patent ductus arteriosus excision of coarctation of the aorta decortication of constrictive pericarditis and the removal of the burden of thyrotoxicosis and similar conditions Other examples are replacement therapy in vitamin or endocrine deficiencies eradication of active infection as in subacute bacterial endocarditis and in some instances of cardiovascular syphilis

PARALDEHYDE

Paraldehyde is a safe and dependable hypnotic with no deleterious effects on the cardiovascular system It is somewhat less certain in its action than chloral hydrate but produces few side reactions Paraldehyde has a very sharp taste and a penetrating and unpleasant fruity odor

It is absorbed rapidly when given by mouth or rectally and can be injected intramuscularly with safety Its acute toxicity is very low and addiction is very rare

Its use in medicine will probably always be limited because of its disagreeable taste and odor Rectal administration in doses of 10 to 20 cc well diluted in water is the usual manner in which it is given It may also be injected intramuscularly in doses of 4 to 8 cc but is likely to cause some pain at the site of injection Paraldehyde is self sterilizing but it should be kept in sterile containers if intended for intramuscular injection

strain for the patient to use a commode or even to go to a nearby bathroom than to conform to a rigid bedpan regimen

All these measures will prove inadequate unless provision is made for mental as well as physical rest Excitement can cause a considerable increase in cardiac work Visitors should be limited in number and should be capable in displaying tact in their conversation and using good judgment during their stay Exciting newspaper articles radio programs and telephone messages should be forbidden while the patient is still in severe congestive failure The regimen just outlined should be maintained until all signs of cardiac failure have disappeared or have become minimal Some form of occupational therapy will be found useful when the patient shows improvement This will restore self confidence and make the patient feel that he is still a useful member of society

There is no fixed plan for getting the patient out of bed The physician must feel his way cautiously with each step The patient may be permitted to hang his feet over the side of the bed on the first day until he becomes fatigued The next and all subsequent steps are taken if no undue dyspnea or rise in pulse rate or other signs of overexertion have occurred The patient is assisted to a comfortable chair placed near the bed on the following day and is permitted to remain there until he becomes tired He may be allowed to get into a chair twice on the following day and is encouraged to take a few steps on the next day This is increased daily until he can get about fairly well provided that no dyspnea or undue rise in pulse rate occurs A week or more will generally be required after a long illness before the patient can be left to his own devices It must be remembered that disappearance of the signs of cardiac failure are merely evidences of improvement but no guarantee against recurrence

Convalescence must be adequate and no undue exertion or coitus should be permitted until complete recovery has occurred A diet low in sodium and avoidance of exposure or undue exertion are important The patient should be instructed to watch for signs of recurrence such as unexplained fatigue palpitation substernal pain or discomfort in the upper abdomen dyspnea unusual arrhythmia or heart rate over eighty per minute Occurrence of any of these requires medical advice but great care and judgment must be exercised not to induce unwarranted anxiety

REST IN BED

It is almost a platitude to say that bed rest is essential in the treatment of heart failure. Rest slows the heart rate and reduces the cardiac output to a fraction of what it would be even at moderate activity. Importance of adequate rest in reducing work of the heart to an absolute minimum is thus apparent. All other measures including digitalis may fail unless the work of the heart is reduced at the same time. The kind and duration of rest will depend on the degree of cardiac failure, its underlying cause and the recuperative power of the patient. Rest in bed should not be carried out in a half hearted manner. It is better to be too strict at the beginning of treatment than to risk an unsuccessful outcome because of inadequate limitation of activities.

BED REST IN SEVERE CONGESTIVE HEART FAILURE

It is best to institute a regimen of *absolute bed rest* in severe congestive heart failure. The patient should assume a position in bed which provides the most comfort. This will generally be some form of semi sitting position since this increases vital capacity and decreases respiratory distress. A special bed which permits a semi sitting position by raising the head and lowering the extremities will be found useful. Pillows or a backrest to elevate the shoulders and head of the patient may be used for the same purpose if a special bed for heart patients is not available but there will be a tendency for the patient to slip down towards the foot of the bed. This may be hindered by fixing a rolled pillow or blanket under the knees of the patient. Another very useful method is to place blocks about 9 inches high under the head of the bed. The patient must be kept as comfortable as possible whatever the arrangement since discomfort induces restlessness and this results in increased effort, a factor which defeats the very purpose of bed rest.

The patient at absolute bed rest is not permitted any active movement. He should be fed by the nurse and should be lifted or moved if a change of position is desired. The use of a bedpan and urinal is mandatory. There are instances when they occasion much discomfort and straining, more perhaps than would result from a commode placed near the bed. The physician will have to exercise considerable judgment in deciding whether it is [illegible]

vices The question of marriage is important and will be discussed later

The value of a rational tempo of living should be explained Rest periods and suitable vacations are advisable for all patients with heart disease Such patients should live in localities at or near sea level certainly at altitudes not exceeding 1500 feet above sea level A warm climate is beneficial but not always necessary The patient should live on the ground floor if possible but one flight of stairs is permissible for patients with fairly well compensated heart lesions

SEDATIVES AND HYPNOTICS

It may be necessary to use sedatives during the day and hypnotics during the night to provide adequate rest There need be no hesitancy in using such measures since sleep and rest are very important to a patient in cardiac failure The beneficial effects of a good night s rest even if artificially induced are frequently surprising

Morphine or one of its allies is the most dependable drug to induce sleep in a patient with cardiac failure To withhold hypnotics from a patient who sleeps poorly serves no purpose and may do harm It was formerly believed that morphine was dangerous in cardiac failure Subsequent experience showed conclusively that this belief was unfounded and that deleterious effects were due to the gravity of the illness rather than to the morphine Barbiturates and other hypnotics are also useful to induce sleep but they are not as dependable as morphine in the earlier stages of treatment when dyspnea and other discomforts interfere with sleep The usual dose of morphine sulfate is 15 mg ($\frac{1}{4}$ grain) subcutaneously unless Cheyne Stokes breathing is present when smaller amounts should be used Other derivatives of opium may be used instead of morphine It is said but certainly not proved that they are less likely to induce nausea and vomiting Hypnotic effects are more certain when opiates are administered subcutaneously These hypnotics may be given every night for about a week without danger of addiction Barbiturates or other sedatives may be used later if necessary

Sedation during the day is indicated if the patient is restless Barbiturates are used widely for this purpose and generally induce satisfactory sedation Caution is necessary in older persons par

on the part of the patient lest he become morbidly overanxious about his illness

REST IN BED IN MODERATE CONGESTIVE HEART FAILURE

Here too the patient is kept in bed as outlined but he may feed himself and some active movements are permitted in bed The use of a bed pan and urinal are advisable The degree of activity permitted while in bed will depend on the progress of recovery but no error will be committed in case of doubt by adopting a conservative attitude The patient may be permitted to get out of bed as described previously when maximum improvement has been attained i e when dyspnea pain or palpitation have disappeared and the heart rate has remained at about 80 beats per minute for several days

Rest in bed as described applies only to patients with actual congestive heart failure Patients with organic heart disease who are not in congestive heart failure should not be confined to bed since it may lead to psychological trauma which will be very difficult to dispel

The care of the patient does not end when he leaves his bed Proper supervision is important after he becomes ambulatory Many problems will require elucidation and frank discussion The patient should be kept at work if possible A sedentary occupation in a sheltered environment is desirable Moderate exercise is permissible provided that it does not cause undue dyspnea fatigue palpitation or other signs of cardiac embarrassment Cycling swimming tennis handball strenuous gymnastics rowing baseball and other sports which are highly competitive or which call for unusual exertion, should be prohibited Walking riding golf minor gymnastics and other moderate sports are permitted provided the patient does not indulge in them during inclement weather or on very hot days The dangers of hot baths and steam baths, sweat cabinets and similar measures should be pointed out Gradual reduction of obesity is very beneficial Coitus must be discussed frankly, especially with men It should be forbidden for several months after cardiac failure or recent myocardial infarction It is dangerous in all forms of coronary disease and especially so in angina pectoris Smoking and alcoholic beverages may be permitted in moderation if the patient is accustomed to such

may be given after maximum improvement is noted and should be continued for the rest of the patient s life The usual daily maintenance dose is 0 065 to 0 1 gm (1 to 1½ grains) of the powdered leaf or its equivalent once a day The dose will vary in different patients and in the same patient from time to time The patient must be seen periodically in order to adjust the dose if signs of failure develop or if toxic manifestations occur The development of toxic symptoms at any stage of treatment will make it necessary to discontinue digitalis for three or four days Maintenance doses may then be resumed or the amount adjusted in accordance with the needs and tolerance of the patient

Adults in fairly severe congestive heart failure may be given 0 13 gm (2 grains) of the powdered leaf or its equivalent three times daily This amount may be maintained until definite improvement is attained after which the individual dose may be reduced to one half until maximum improvement Maintenance doses may then be continued daily as described

Adults in moderate congestive heart failure may be given 0 1 gm (1½ grains) of the powdered leaf or its equivalent three times daily until maximum improvement or until toxic symptoms occur after which maintenance doses may be used as described

Digitalis should be administered orally unless some definite indication exists for use of a different route Nausea or vomiting when due to cardiac failure and obvious congestion of the liver or gastro intestinal tract may interfere with absorption of digitalis when taken orally Rectal administration is useful in such instances The entire daily requirement of a liquid preparation such as the tincture may be diluted in about 3 ounces of tap water and instilled high in the rectum after a cleansing enema The dose used rectally is the same as that used by mouth absorption is fairly rapid and enough bypasses the congested liver and gastro intestinal tract to produce a favorable effect Rectal administration may be used daily until oral use is practicable Suppositories containing digitalis are also useful but it is not certain that absorption is as good as that obtained from instillation of liquid preparations Rectal administration of digitalis may also prove useful in patients who state that they become nauseated or vomit or that they cannot tolerate digitalis Such patients may tolerate large doses of digitalis rectally if they are not told that the drug is being administered

ticularly those with cerebral arteriosclerosis, since they may develop mental disturbances such as disorientation, restlessness or delirium when barbiturates or bromides are used Phenobarbital in doses of 16 to 32 mg (¼ to ½ grain) three times daily is usually sufficient to provide relaxation Other barbiturates in corresponding doses are equally satisfactory but not superior to phenobarbital Bromides in any form in doses of 1 gm (15 grains) two or three times daily are equally satisfactory Here, too older patients must be watched for mental symptoms low grade fever and skin eruptions if the bromides are used for any length of time Chloral hydrate is not dangerous in heart failure but has a bad taste and is not superior to barbiturates or bromides Paraldehyde is very effective but leaves a very objectionable odor after oral rectal or intramuscular use

DIGITALIS

Digitalis or one of its allies is indicated in all cases of congestive heart failure regardless of the heart rate or whether auricular fibrillation is present or not The initial dose should be determined by the degree of failure and subsequent dosage will depend upon the response Enough must be given to induce maximum improvement provided the heart is capable of such a response

Adults in very severe congestive heart failure will generally require about 0 6 gm (9 grains) of the powdered leaf or 6 cc (90 minims) by measure of the tincture on the first day of treatment Smaller amounts may be sufficient if the patient has already been taking digitalis This total daily ration may be taken as one dose or it may be divided in three equal portions and given at six hourly intervals The amount required the next day will be determined by the results obtained but two doses of 0 2 gm (3 grains) each may be continued until definite improvement appears as manifested by considerable slowing of the heart rate onset of diuresis decrease of dyspnea or lessening of the hepatic tenderness This may take one to three days with the foregoing dosage rarely longer Persistence with such large doses until compensation is restored fully may result in toxic symptoms Definite improvement when it occurs should be regarded as a signal to reduce the individual dose to one half until further improvement occurs This will generally take two or three days seldom longer unless signs of digitalis intoxication develop A daily maintenance dose

Other preparations of digitalis or its allies may be used if standard preparations are not well tolerated Great interest is being displayed in preparations of digitoxin and of digitalis lanata Many of these have been shown to be the equal of ordinary digitalis but none has proved superior Detailed information relative to the action dosage and use of these and other preparations are found in the chapter dealing with the pharmacology of digitalis

There are very few contraindications to the use of digitalis in congestive heart failure Stokes Adams syndrome when due to incomplete heart block may be made worse by digitalis Toxic manifestations of digitalis including heart block extrasystoles and paroxysmal ventricular tachycardia require that the drug be discontinued for three or four days unless congestive failure is still present in which event digitalis may be continued but with great care Heart block which is due to inherent disease of the myocardium or to congestive failure may be improved by digitalis Even large doses may be used in such instances without danger of aggravating the block Acute myocardial infarction is generally considered a contraindication to the use of digitalis but it should be given in the presence of frank congestive failure The serious consequences of such heart failure outweigh all hypothetical dangers such as ectopic beats rupture of the heart emboli or changes in the clotting time of the blood I have used large doses of digitalis and strophanthin without deleterious results in congestive heart failure following acute myocardial infarction The use of digitalis is generally considered unwise if emboli have occurred in the course of heart failure but careful studies do not support the opinion that digitalis alone was a factor since emboli are just as frequent when no digitalis is used It is hardly necessary to mention that hypertension and insufficiency of the aortic valve are no longer considered contraindications to the use of digitalis

DIURETICS

Diuretics will be indispensable if bed rest and digitalis fail to afford relief from pulmonary or hepatic congestion edema serous effusion nocturnal paroxysmal dyspnea or acute pulmonary edema It is good practice if the foregoing are severe to use diuretics at the very beginning of treatment in order to spare the patient as much discomfort as possible It is also wise to remove large pleural effusions by aspiration at the beginning of treatment

Intravenous administration of digitalis preparations or its allies is used chiefly in cardiac emergencies or in severe failure where absorption from the gastro intestinal tract, including the rectum, is uncertain or too slow

An initial injection, equivalent to 6 grains (0 4 gm) of the powdered leaf or 4 cat units may be given if the patient has received no digitalis during the preceding three or four days Another intravenous injection of one half this amount may be given in six hours if necessary Smaller doses should be used if the patient who is still in failure has been getting digitalis The equivalent of 0 2 gm (3 grains) or 2 cat units of the powdered leaf may be injected intravenously every four hours in the latter group of patients until definite improvement is attained or toxic symptoms develop Oral administration should be instituted as soon as the emergency has passed or absorption from the gastro intestinal tract becomes more certain

Strophanthin produces all of the effects of digitalis but acts rapidly and is eliminated quickly It can be administered only by intravenous injection It is a safe and dependable remedy for parenteral use when rapid action is necessary or where absorption after oral administration is uncertain It must not be used in patients who have received digitalis in the preceding three or four days or in those who are well digitalized Failure to observe this precaution can result in very rapid additive effects with toxic symptoms and serious accidents The indications for strophanthin are the same as those for preparations of digitalis which are injected intravenously Strophanthin is eliminated more rapidly hence cumulative action is less likely Several varieties of strophanthin and ouabain are available but Strophanthin K will prove the most useful The initial intravenous dose is 0 25 to 0 50 mg , depending on the urgency and severity of the failure It is well to dilute the strophanthin in 10 cc of dextrose solution and to inject slowly Another dose of 0 25 mg may be injected in six hours if necessary but a total of 0 75 mg during the first day should not be exceeded The effects may be maintained by further daily injections of 0 25 mg seldom 0 50 mg , but it is better to return to oral administration of maintenance doses of digitalis as soon as possible The first maintenance dose of about 0 1 gm (1½ grains) of digitalis may be given almost immediately after the last injection of strophanthin

precautions are taken Known sensitivity to mercury precludes the use of such diuretics Mercurial diuretics should not be used in active nephritis impending uremia, severe anemia cachexia and ulcerative conditions of the bowels Caution should be exercised in prostatic obstruction and in gout since acute urinary retention or an acute attack of gout may be precipitated Albuminuria or red blood cells in the urine if the result of congestive heart failure are not contraindications to the use of mercurials Diuresis after either intravenous or intramuscular injection may be so copious that marked weakness painful cramps in the voluntary muscles or mental symptoms may occur These may be avoided by using smaller doses more frequently if necessary Digitalis is retained in edema fluid and serous effusions and is liberated into the blood stream during diuresis Enough digitalis may be liberated in this manner to cause toxic symptoms This complication is described in greater detail in the chapter on digitalis

The smallest effective dose by either route is generally 1 cc and is the amount which is given as a test dose initially to determine the response and possible sensitivity Larger amounts 1 5 or 2 cc are often used to induce adequate diuresis The required amount may be given at intervals of three days or at longer intervals until edema congestion or paroxysmal dyspnea disappear It is frequently necessary to continue injections generally at longer intervals after the patient becomes ambulatory in order to prevent recurrence of symptoms Mercurial diuretics may be used almost indefinitely without harm to the patient

Suppositories containing the same mercurial diuretics may be used The results are neither as certain nor as good as those obtained with intravenous or intramuscular injection Troublesome proctitis may develop which prevents further use of this method Oral administration of mercurial diuretics has not proved satisfactory and is often followed by abdominal pain and severe gastrointestinal disturbances

The effects of mercurial diuretics can be enhanced greatly by oral administration of ammonium chloride Ammonium nitrate or potassium nitrate may also be used for the same purpose Two grams (30 grains) of any of these are given three or four times daily as enteric coated pills A useful method is to give any of these preparations one day before on the day of the injection and for two days after administration of the mercurial

since they cause much discomfort and are absorbed very slowly even if mercurial diuretics are used

Xanthines have been used for many years as diuretics They are not as reliable or as effective as mercurial diuretics and they frequently cause digestive disturbances if used for any length of time Theobromine sodium salicylate may be given in doses of 1 gm (15 grains) three times a day or a similar amount may be given every hour for four doses daily The latter method can be repeated at intervals of three or four days Theophylline in 0 3 gm (5 grains) doses or theobromine calcium salicylate in doses of 0 5 to 1 gm (7½ to 15 grains) may be used three times daily for the same purpose There is no denying that these and other xanthines exert a good diuretic action in experimental animals and in some patients but they cannot compare with mercurial diuretics

Mercurial Diuretics are reliable and very potent and are indicated where copious diuresis is necessary Mercuhydrin mercupurin and salyrgan theophylline are the preparations generally used They are equally potent and the dosage and routes of administration are the same for all three Intravenous administration is preferable since it results in slightly better diuresis and causes no pain unless some of the solution leaks into the tissues outside the veins There are some reports of untoward reactions and a few deaths following intravenous injection of mercurial diuretics but this need not deter the physician since the incidence of such reactions is no greater than with arsenicals in the treatment of syphilis There are certain manifestations which should serve as a warning that intravenous injections are not well tolerated and that intramuscular injection should be used instead in that patient Such symptoms are headache fever skin eruptions thoracic oppression chills and pulmonary edema

Intramuscular injection of the same amount of mercurial diuretic results in diuresis almost as copious as that obtained with intravenous administration No serious accidents are reported from intramuscular injections although variable degrees of pain are often produced at the site of injection The addition of procaine or other local anesthetic to the diuretic is not very effective in preventing such pain

Untoward reactions are encountered occasionally after any mercurial diuretic Many of these can be prevented if the proper

much fluids as he wishes although it is wise not to allow fluids after supper if paroxysmal nocturnal dyspnea or pulmonary edema are likely to occur. Severe restriction of fluids is unnecessary since it has been shown that it is the intake of sodium rather than of fluids which favors the occurrence or persistence of edema or congestion. The above described diet may be maintained as long as the patient remains in bed unless weakness or hunger develop. The caloric intake must then be adjusted in accordance with the needs of the individual patient.

Various modifications may be desirable under certain circumstances. Diets of less than 1200 calories may prove useful if there is reason to reduce the weight of obese patients. Diets of 800 calories have been used in such instances especially in the presence of hypertension or angina pectoris. Low caloric diets reduce the metabolic rates after about two weeks and this, in turn, reduces the work of the heart. Patients who experience distress after meals may obtain relief if smaller meals are served more often if necessary. Flatulence may be controlled by limiting the rations of bulky vegetables such as cabbage, sauer kraut, raw tomatoes, celery, lettuce and excessive use of salads. Charged drinks, especially if ice cold, may cause distress. There are patients in whom fresh milk causes flatulence and other forms of abdominal distress. Reduction or complete elimination of milk in such patients often results in prompt relief.

TREATMENT OF SPECIAL FEATURES

NAUSEA AND VOMITING

These may be due to passive congestion of the gastro intestinal tract or liver. More aggressive treatment of the cardiac failure and larger amounts of digitalis will be indicated. Similar effects may be due to local irritation of the stomach by standard preparations of digitalis or to reflex toxic action from excess dosage. Digitalis must be discontinued for four or five days in the latter instance and rectal or parenteral injection may be used if digitalis irritates the stomach by local action. It is stated that digitoxin is not irritating to the stomach, hence it may be used instead of standard preparations of digitalis in such instances. Other measures are necessary if none of the foregoing causes are at fault. All food and fluid should be discontinued for twenty four or

Diuresis generally begins two to four hours after injection and passes its maximum in twelve hours although there are many exceptions The diuretic effect seldom lasts longer than twenty four hours

Mercurial diuretics may fail to act for a number of reasons The patient may be in a terminal state or his capacity for diuresis may have become very limited due to absence of renal reserve Depletion of blood proteins or electrolytes the intake of large amounts of sodium or the use of alkalies may interfere with the action of mercurial diuretics The use of opiates sometimes reduces the diuretic response Diuresis may again set in if any of the foregoing factors can be eliminated Success may sometimes be attained if edema or serous effusions are first drained mechanically An increase of the amount of mercurial diuretic to as much as 4 cc intravenously may sometimes prove effective when smaller doses fail Diuretics may sometimes fail after prolonged use for no discernible reason A rest period during which no mercurial is used for two or three weeks should then be tried An intravenous injection after such a rest period may then be followed by satisfactory diuresis

DIET

The work of the heart is increased appreciably by intake of food Hence the diet should be so regulated that nutritional requirements are met with minimal demands on the heart Treatment of severe congestive heart failure may be initiated with a modified Karell diet consisting of a glassful of milk four times a day for two days No other food or fluid is given during this time A similar amount of fruit juices or a kilogram of easily digested fruit may be substituted if milk is not tolerated by the patient The intake of salt and fluid is maintained at a low level by this regimen Excellent results may be obtained in some patients, especially in the presence of severe congestion of the lungs and liver or in severe edema

A well balanced appetizing diet of 1200 calories daily may be used in moderate cardiac failure or after the patient has already been on a Karell regimen for two days The salt content should be low not more than 2 or 3 gm daily including the salt added during cooking No additional salt for seasoning should be served with the meals The patient should be permitted to drink as

The tent is arranged by tucking its skirts under the mattress at the head and sides of the bed and the front is placed under a draw sheet tucked tightly across the patient and under the mattress at each side It is important to close all leaks in order to prevent loss of oxygen The flow of oxygen is then turned on at 15 liters per minute for thirty minutes in order to provide a concentration of about 50 per cent within the tent A similar flow should be used for ten to fifteen minutes after the tent is opened for nursing or other care in order to maintain the concentration of oxygen The flow may be reduced to 8 or 10 liters per minute

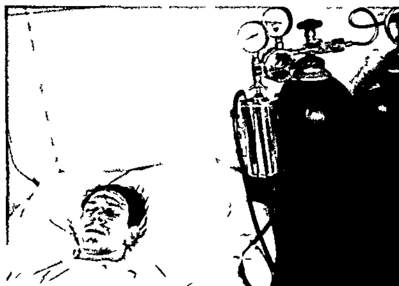


Fig 5—Arrangement for administration of oxygen by nasal catheter

to maintain the concentration at 40 to 50 per cent The concentration of oxygen should be checked at least once daily in order to make certain that the patient is deriving the full benefit of oxygen therapy

Administration of oxygen should be continued as long as necessary The average patient will require from five to seven days of oxygen therapy No form of oxygen therapy should be discontinued abruptly but the concentration should be lowered by 10 to 15 per cent every two days until a concentration of about 30 per cent is reached after which administration of oxygen may be discontinued

thirty six hours A cleansing enema is given after which chloral hydrate 1 gm with sodium bromide 2 gm in about 4 ounces of water is instilled high up in the rectum as a retention enema The patient is permitted sips of ginger ale, tea milk, or broth next day and the diet is then built up gradually in accordance with the tolerance of the patient

CONSTIPATION

This may become troublesome while the patient is in bed Mild laxatives such as an ounce of mineral oil, a teaspoonful or two of aromatic cascara or of milk of magnesia at night might suffice A small plain water enema of about 500 cc or of a similar amount of soap suds may be given every other morning if laxatives are not effective Mineral oil should not be used for too long a period of time since it may induce flatulence and abdominal distress The patient should be watched so that he does not aspirate oil down his trachea since this has given rise to lipoid pneumonia

SEVERE DYSPNEA AND CYANOSIS

Oxygen therapy is of great value in the relief of severe dyspnea or cyanosis or when these manifestations do not respond to routine treatment of congestive heart failure Oxygen therapy should be continuous until no longer needed Interrupted administration of oxygen is wasteful and of little or no value

It is necessary of course to re examine the patient carefully in such instances for possible complicating factors which may be responsible for severe or persistent dyspnea or cyanosis Such factors are pleural effusion pulmonary infarction, pneumonia severe emphysema extensive bronchitis bronchial asthma pericardial effusion renal disease or abdominal distention Pleural or pericardial effusion if responsible should be removed by paracentesis at once and other factors should be treated appropriately without delay

Oxygen may be administered by various methods depending upon the degree of dyspnea or cyanosis The oxygen tent (see Fig 1, page 43) is a useful method of administration and has the additional advantage that the temperature and humidity within the tent can be regulated in accordance with the needs of the patient Concentrations of oxygen ranging from 40 to 60 per cent can be maintained continuously for as long a time as necessary

may use it himself whenever needed Oral administration is generally ineffective and may produce gastro intestinal disturbances

Other measures may prove useful if aminophylline fails Oxygen administered by tent or catheter may prove successful but this must be continued since periodic breathing will return as soon as oxygen is discontinued Small doses of morphine 8 mg (1/8 grain) or one of its allies may be used but care should be taken that the respiratory center is not depressed too much with further exaggeration of the periodic breathing It is wise in all instances to check on the daily intake of codeine sedatives and hypnotics to see if they are responsible for the periodic breathing

PAROXYSMAL NOCTURNAL DYSPNEA (CARDIAC ASTHMA)

This form of nocturnal dyspnea may cause great discomfort at night and may interfere seriously with sleep It must be distinguished from ordinary orthopnea caused by the patient slipping down from his pillow during sleep

Treatment of an attack consists of placing the patient in a semi sitting or upright position immediately A subcutaneous or intramuscular injection of morphine 16 mg (1/4 grain) or one of its allies together with 0 6 mg (1/100 grain) of atropine should be given at once This will generally provide relief but it may be necessary to use additional measures such as oxygen by tent or catheter

Prompt and adequate digitalization is indicated if this has not been done before Strophanthin K 0 5 mg may be injected intravenously if the patient has not received digitalis during the preceding four days The equivalent of 0 2 gm (3 grains or 2 cat units) of a digitalis preparation may be injected intravenously if the patient has been taking digitalis up to the time of the attack This may be repeated in two hours and again in six hours unless signs of digitalis toxicity develop Maintenance doses of digitalis are then given orally as described

ACUTE PULMONARY EDEMA

Acute pulmonary edema manifesting itself as dyspnea wheezing respirations frothy sputum which is pinkish or bloody and many crepitant and wheezing rales throughout both lung fields is an emergency which requires prompt treatment The patient should receive morphine and atropine as described under paroxysmal

Oxygen may also be administered by *nasal catheter* Oxygen is fed from a tank through a humidifying apparatus to an ordinary No 10 French catheter the terminal inch having several small perforations in order to disperse the flow of oxygen in the pharynx The catheter should be well lubricated and passed through the nose into the pharynx until the patient begins to swallow oxygen The catheter is then withdrawn a little until its end is behind the lower part of the uvula It is then fastened with adhesive tape to the forehead and bridge of the nose A flow of about 6 liters per minute will provide an oxygen concentration of about 45 per cent The catheter should be changed every twelve hours and the used one should be washed cleaned and boiled until needed again Irritation of the nasopharynx may result if frequent change of catheter is neglected

Very severe dyspnea or cyanosis may require concentrations of *95 to 100 per cent oxygen* (See Fig 3 page 45) This may be administered with a *BLB mask* devised by Boothby Lovelace and Bulbulian Such concentrations of oxygen may be used for as long as twenty four or forty eight hours after which lower con centrations may be given by tent or catheter A flow of 8 to 12 liters per minute will generally be necessary to maintain such high concentrations of oxygen

CHEYNE STOKES RESPIRATION

Cheyne Stokes respiration occurs normally during sleep but may become greatly exaggerated in congestive heart failure The periods of apnea may become so long and the succeeding hyperp nea so violent that sleep is disturbed Intravenous injection of 0 24 to 0 48 gm (4 to 7½ grains) of aminophylline (theophylline ethylenediamine) in 20 cc of dextrose solution usually abolishes such disturbing breathing promptly The injection should be made slowly in order to reduce the possibility of headache uncomfort able flushing or thoracic oppression A similar injection may be given before bed time in order to prevent the occurrence of ex aggerated Cheyne Stokes breathing later in the night Intra muscular injection of the same dose may serve equally well but is generally painful Rectal administration of 0 5 to 1 gm in the form of a suppository or as a solution after a cleansing enema at bed time frequently prevents severe Cheyne Stokes respiration This method if successful, has the advantage that the patient

in the extremities and thus to reduce the load on the heart This procedure has been recommended highly but my own experience with it has been disappointing

Intravenous injection of 50 cc of 50 per cent dextrose solution with and without 0 48 gm of aminophylline has been used with favorable results It is questionable how valuable such therapy will be if the measures previously discussed fail

Subsequent attacks of cardiac asthma and pulmonary edema may often be prevented by intensive cardiac therapy particularly by strict bed rest Periodic use of mercurial diuretics sufficient to eradicate all signs of pulmonary and hepatic congestion may also prevent attacks

PLEURAL EFFUSION

Pleural effusion may be responsible for severe or persistent dyspnea or cyanosis and is best removed by thoracentesis early in the course of treatment Such effusions respond rather slowly to digitalis and diuretics and much discomfort will be avoided if the fluid is removed by paracentesis rather than by the much slower process of digitalization and diuresis The usual site for thoracentesis is in the eighth or ninth interspace just below the angle of the scapula and well within the area of dullness A sitting position is preferable but the patient may rest on the side opposite the effusion while being supported in a semi sitting position by pillows The site of puncture is cleaned and painted with an antiseptic solution A 1 or 2 per cent procaine solution is then injected intradermally and a 21 or 22 gauge needle attached to a syringe containing anesthetizing solution is then pushed in The deeper structures are then anesthetized and a needle about 2 inches long is then pushed through until resistance diminishes abruptly This is usually the pleural cavity The plunger is partially withdrawn to see if fluid can be obtained at that level or if it is necessary to insert the needle more deeply The needle may then be connected by a three way stopcock to a large syringe or to a suction apparatus and about 500 to 800 cc of fluid is removed The needle should be tilted in various directions the patient being asked to cough or air may be forced in to free the needle from possible plugs of fibrin if the flow is not satisfactory Undue weakness pain or cough are signs that aspiration should be discontinued Collapse or pleural shock is best treated by intra

nocturnal dyspnea and rapid digitalization should be carried out if this has not been done before The administration of 100 per cent oxygen under positive pressure is invaluable and may result in disappearance of pulmonary edema within a very short time A Meter mask is used which enables the patient to exhale under a positive pressure of 1 2 3 or 4 cm of water Such pressures *counteract the tendency of fluid to exude into the alveoli A flow* of 10 to 12 liters per minute is used with this mask in order to obtain an oxygen concentration of about 100 per cent Care must be taken to prevent complete collapse of the collecting bag during respiration It will be useful to begin with a positive pressure of 1 cm of water and to increase this pressure by 1 cm every five or ten minutes until pressures of 3 or 4 cm of water are attained This pressure is maintained until the lungs become clear after which the pressure may be reduced by 1 cm every two or three hours Return of pulmonary congestion will necessitate reapplication of the mask in the manner described at the beginning of treatment Oxygen may then be administered by tent or nasal catheter after the Meter mask is no longer required

The foregoing measures will prove adequate in the great majority of cases of acute pulmonary edema due to congestive heart failure Venesection may provide rapid and striking relief A constrictor is placed about the arm sufficient to compress the brachial veins without obstructing the arteries The vein in or just below the bend of the elbow may be opened with a scalpel *permitting the blood to flow freely in a basin held under the* arm, or this may be accomplished by inserting a large bore needle into the vein From 500 to 700 cc of blood may thus be removed rapidly from the basilic or cephalic vein A suction bottle or negative pressure apparatus may be connected to the needle to facilitate rapid flow of blood The constrictor is then removed and a gauze dressing held in place by adhesive tape is applied So called bloodless venesection is performed by applying constrictors high up on all four extremities Sufficient compression is applied to prevent venous return to the heart without impeding arterial flow This is done by applying cuffs of a sphygmomanometer under a pressure just above the diastolic arterial blood pressure Compression is maintained for about thirty minutes and the constrictors are *then released one by one The principle of* this procedure is to trap an appreciable amount of venous blood

The dietetic regimen suggested by Kempner may prove useful in such instances It consists essentially of rice, fruits and about 1000 cc of fruit juices and nothing else The sodium content is very low and the caloric requirements are easily met Details of this diet are described fully under treatment of hypertension Particular attention should be paid to elimination of sodium chloride sodium bicarbonate and sodium salts of all drugs used in treatment

Mechanical removal of persistent edema is indicated if the fore going procedures fail The patient is placed in a chair or his feet are lowered while still in bed and the skin on the dorsum of the feet and lower part of the legs is cleaned carefully An antiseptic solution is applied and from two to four incisions each about 2 inches long are made into the subcutaneous tissue of both lower extremities Local anesthesia may be used along the lines of in cision although this is sometimes not necessary Copious sterile absorbent dressings are applied over the incisions and the legs are permitted to hang down in order to favor drainage Large amounts of fluid may escape although the flow is likely to decrease or stop several hours after the incisions are made It is an inter esting fact that the flow may become quite profuse after ad ministration of mercurial diuretics It has also been noted that mercurial diuretics may again become effective after mechanical removal of edema if diuresis was unsatisfactory before such drain age Southey s tubes or other large bore needles may be intro duced into the subcutaneous tissues and connected with long rubber tubing to receiving bottles placed on the floor It is an excellent method when it works but the needle frequently become plugged or obstructed by clotted material hence its usefulness is very limited It may be necessary to clean the needles and re insert them in different locations when the flow becomes un satisfactory

PULMONARY INFARCTION

Pulmonary infarction is usually due to emboli originating either in the right side of the heart or in the veins of the lower extremities Conservative treatment is the method of choice unless there is unequivocal evidence that the iliac veins or the veins of the lower extremities are at fault Ligation of the offending veins then comes into consideration

Conservative treatment consists of immediate subcutaneous in

muscular injection of 0 5 to 1 cc of 1 1000 solution of epinephrine Such shock is not likely unless the patient is very weak or seriously ill or too much fluid is removed at one sitting The degree of relief does not depend on the exact amount of fluid removed hence it is not wise to drain the pleural cavity completely at any one sitting

PERICARDIAL EFFUSION

Aspiration of the pericardium will be necessary only if the effusion is copious and interferes with cardiac function The same aseptic precautions and anesthesia will be necessary as in pleural paracentesis Several methods are available and these are de scribed *in the chapter dealing with the treatment of pericarditis* Here only the route most frequently used will be discussed The patient is placed on his back in a semi sitting position The usual site of puncture lies in the fifth interspace about 1 or 2 cm inside the left border of cardiac dullness The skin and deeper tissues are anesthetized with a 1 or 2 per cent procaine solution A 16 gauge needle about 2½ inches long is then attached to a syringe containing about 5 or more cc of procaine solution This needle is pushed through the chosen site in an upward and backward direction toward the spine This is done by short jabs with infil tration at each step in order to provide anesthesia during the time the needle is being pushed into the pericardium The peri cardium is entered when resistance to the needle decreases as though it reached a cavity Aspiration should be attempted when the pericardium is entered and the needle should be tilted in a direction parallel to the surface of the heart with the point down wards as soon as fluid is obtained This will prevent unnecessary laceration of the surface of the heart The pulsations of the heart can be felt via the needle but need cause no concern since no harm will be done even if the ventricle is actually punctured No attempt should be made to aspirate all of the fluid since this may lead to collapse From 300 to 500 cc are sufficient even with large pericardial effusions since relief is marked and the process can be repeated on the next or subsequent days if necessary

PERSISTENT EDEMA

Edema sometimes persists in spite of adequate bed rest digitalis and diuretics It is necessary in such instances to check the intake of sodium in any form and to reduce this to an absolute minimum

BRONCHOPNEUMONIA

Bronchopneumonia is always a serious complication, especially in old patients It is easily overlooked since the symptoms, signs and roentgenologic manifestations closely resemble those produced by pulmonary congestion

The treatment of cardiac failure in such patients must not be relaxed in fact it should be intensified It must be remembered in this connection that the efficacy of digitalis and its allies is reduced by the presence of fever and that larger doses may be necessary

Penicillin is indicated as soon as the diagnosis of pneumonia is made Intramuscular injections of 30 000 units of penicillin should be given every three hours day and night until no fever is present for about three days Sulfonamides may be used but are more likely to cause untoward reactions Sulfadiazine 2 gm may be given at once and the same amount may be repeated in four hours Subsequent doses of 1 gm are then given every four hours day and night until fever is absent for two days and then every eight hours for two more days before the drug is discontinued Other sulfonamides may be used of course Fluid intake should be ample to provide a urinary output of at least 1500 cc daily in order to prevent renal complications



jection of 16 mg ($\frac{1}{4}$ grain) of morphine sulfate with 0 6 mg (1/100 grain) of atropine sulfate Pain, cough and dyspnea are thus allayed and danger of further emboli is reduced by providing comfort and relaxation Intravenous or intramuscular injection of papaverine *hydrochloride in doses of 32 to 65 mg* ($\frac{1}{2}$ to 1 grain) with *atropine sulfate 0 6 mg (1/100 grain) may* also be given although there is no convincing evidence that papaverine is of great benefit in such instances Absolute bed rest and oxygen if necessary are of decided benefit

The value of anticoagulants is still a matter of debate They can be of value in preventing further clotting either at the site of origin or in the region of the infarct but the effect on the infarct itself is doubtful Anticoagulants should never be used unless the prothrombin time of the blood can be estimated daily These considerations and the fact that anticoagulants are not always innocuous create a certain degree of hesitancy in regard to their use as a routine measure

The question whether digitalis should be discontinued is not easily answered It is customary to stop the use of digitalis if infarcts occur in the lungs or elsewhere It has never been proved conclusively however that digitalis is actually responsible for detachment of thrombi from the walls of the right side of the heart Thrombi are more likely to be detached by restlessness or movement of the patient They are also more likely to form during cardiac failure The best plan is to maintain good cardiac function with as much digitalis as is necessary since this will hardly result in loosening of additional mural thrombi and can do no possible harm if the emboli arise from thrombosed peripheral veins

It will be wise to keep the patient at absolute bed rest for at least two weeks after the temperature has become normal The patient may then be permitted to get out of bed gradually in order to decrease the possibility that more emboli will be detached by precipitate movement

Recurrent pulmonary infarction when associated with cardiac arrhythmia may sometimes be improved by use of quinidine It is not clear why a normal rhythm should not give rise to emboli if there are mural thrombi in the heart but this has been our experience in several instances The method of administering quinidine in cardiac arrhythmia is described in the chapter dealing with auricular fibrillation

3

DISEASES OF THE CORONARY ARTERIES

TREATMENT OF ACUTE MYOCARDIAL INFARCTION (CORONARY THROMBOSIS)

There are three objectives in the treatment of acute myocardial infarction These are relief of pain and other symptoms during the early stages of the attack provision of adequate rest until reparative processes in the infarcted area are fairly well advanced and constant watch during the entire course of treatment for recurrence extension or other complications

THE IMMEDIATE TREATMENT OF THE ATTACK

The patient should be placed immediately at absolute bed res or moved to a hospital by ambulance for better care Morphine sulfate 15 mg (¼ grain) or one of its allies should be injected subcutaneously at once for relief of pain This may be repeated in fifteen minutes if necessary It may be necessary in some in stances to give additional injections at half hourly intervals but the total dosage should not exceed 65 mg (1 grain) Morphine may be injected intravenously if the pain is very severe A tablet of morphine sulfate containing 15 mg (¼ grain) is dissolved in about 2 cc of boiled water The solution is drawn up in a syringe and injected intravenously very slowly drop by drop until definite relief of pain is attained The injection is then discontinued even if less than the full amount has been given since the sedative effects are profound and are initiated very quickly Additional measures such as slow intravenous injection of 0 5 gm (7½ grains) of aminophylline or inhalation of 100 per cent oxygen by a BLB or other special mask may occasionally afford relief when mor phine alone fails

may lead the patient to believe that he is more seriously ill than is actually the case The indications for oxygen therapy in acute myocardial infarction are marked dyspnea, cyanosis edema of the lungs or restlessness These distressing symptoms are often greatly relieved by oxygen so that the patient soon becomes much more comfortable and may even drop off to sleep It is not known if oxygen has any direct beneficial effect on the heart or infarcted area but the symptomatic relief and clinical improvement which follow its employment amply justify its use when indicated The methods of administration are the same as in congestive heart failure and are described on pages 66 67, 68 and 70

Sedatives

Sedatives are frequently necessary, especially during the earlier stages of treatment Morphine or its allies may be used for pain or severe discomfort if necessary The danger of addiction is not great and can always be treated after the patient has recovered from the attack of myocardial infarction Phenobarbital 15 to 30 mg (¼ to ½ grain) three times a day orally or a bromide in doses of 1 gm (15 grains) several times daily will generally suffice if the patient is restless

Quinidine

The administration of quinidine sulfate in doses of 0 2 gm (3 grains) three or four times daily during the first two or three weeks after the onset of the attack has been recommended in order to prevent serious arrhythmia There are no well controlled studies to prove the value of this measure clinically The procedure is harmless unless severe congestive failure develops and it may be used until further clinical observation determines its actual value

Xanthines

It is customary to administer xanthines to patients with acute myocardial infarction It is a ritual which is practiced universally but there is no unequivocal experimental or clinical evidence that orally administered xanthines exert beneficial effects Aminophylline in doses of 0 1 to 0 2 gm (1½ to 3 grains) or theobromine calcium salicylate in doses of 0 5 gm (7½ grains) three times daily may be used Other preparations may also be employed but the physician should watch for untoward effects such as nausea

SUBSEQUENT TREATMENT

Rest in Bed

Absolute rest in bed as described on page 52 is necessary for all patients This is continued for about three weeks for the average patient but longer periods may be necessary for very severe attacks or if recovery has been unsatisfactory The patient should remain in bed for three more weeks after this but he may now be permitted some active movement in bed and may feed himself He is permitted to get out of bed as described on page 55 after this additional three weeks if pain and other discomfort are no longer present

The patient should spend at least three more weeks at home during which time he may go to the bathroom and walk about the house He may be permitted to go out of doors at the end of this time if the weather is favorable Light work may be attempted about three months after the onset of his illness provided recovery has been satisfactory He may begin with about two hours at some sedentary occupation on the first day and increase this by one hour daily until an eight hour day has been attained provided this is well tolerated Further activity will depend on the patient s tolerance and freedom from symptoms rather than on any fixed schedule The aim should be to restore the patient to a useful occupation preferably sedentary in nature, so that he will consider himself a useful member of society

It is important that the physician and relatives maintain an air of cheerfulness and confidence throughout the entire course of treatment All patients realize that myocardial infarction is a serious illness and some are aware that serious accidents including sudden death are possible The lengthy course of treatment and the strict precautions may arouse fear It is difficult for many patients to preserve a sense of equanimity in such circumstances especially if the patient has an unstable emotional system Great skill and tact as well as constant encouragement will be necessary to prevent misinterpretation by the patient of any unusual subjective symptom which he may experience It is very easy for the patient to develop an anxiety neurosis which may cause more unpleasant difficulties than the myocardial infarction itself

Oxygen Therapy

Oxygen should not be used unless definitely indicated since it

may lead the patient to believe that he is more seriously ill than is actually the case The indications for oxygen therapy in acute myocardial infarction are marked dyspnea, cyanosis, edema of the lungs or restlessness These distressing symptoms are often greatly relieved by oxygen so that the patient soon becomes much more comfortable and may even drop off to sleep It is not known if oxygen has any direct beneficial effect on the heart or infarcted area but the symptomatic relief and clinical improvement which follow its employment amply justify its use when indicated The methods of administration are the same as in congestive heart failure and are described on pages 66, 67 68 and 70

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anorexia and epigastric distress which any xanthine can induce, even if given as enteric coated pills

Papaverine has been shown to dilate coronary arteries and to have other beneficial effects similar to those attributed to xanthines It is administered orally as papaverine hydrochloride in doses of 30 to 65 mg ($\frac{1}{2}$ to 1 grain) three or more times daily The same amounts may be given by intramuscular or intravenous injection but there is as yet insufficient controlled evidence for proper evaluation of papaverine in clinical practice

Anticoagulants

It is well known that there may be an extension of the original thrombus in the coronary artery that thrombosis may occur in other branches of the coronary tree or that mural thrombi may form on the endocardial surface of the infarcted area These may occur at any time after the initial attack and may lead to serious consequences including sudden death It seems logical to employ anticoagulants during the course of treatment in order to prevent such complications Several authors report that the death rate can be reduced and the incidence of complications such as emboli can be lowered by the use of anticoagulants No definite conclusions can be drawn until larger groups of patients and adequate controls have been studied

Dicumarol is the anticoagulant of choice at present for this purpose but no anticoagulant should be used unless the prothrombin time can be checked accurately every day The prothrombin time should be determined immediately after the attack by the Link Shapiro dilution modification of the Quick method and every morning thereafter as long as dicumarol is being administered An initial dose of 300 mg of dicumarol is given orally on the first day after prothrombin time is determined Doses of 200 mg are given on subsequent days providing the prothrombin time that morning is greater than 20 per cent of normal No dicumarol is given on any day when the prothrombin time is less than 20 per cent of normal The daily maintenance dose is generally 100 mg but varies greatly Enough should be given to maintain the prothrombin time at about 20 per cent of normal for as long as the patient remains in bed Sensitivity to dicumarol or bleeding may be controlled by one or more transfusions of 500 cc of freshly drawn blood which may be citrated and by

intravenous injection of 60 mg of menadione bisulfite Dicumarol should not be used in the presence of definite renal or hepatic insufficiency purpura subacute bacterial endocarditis or blood dyscrasias with a tendency to hemorrhage

Diet and Fluids

A well balanced diet divided in smaller portions and served more often if necessary will meet most requirements The patient will eat very little during the first few days of his illness and he should not be urged to take more than he desires A low caloric diet reduces the work of the heart by decreasing metabolism A caloric intake of 1200 calories or less daily will be ample for most patients while they are still in bed Spices and salt content should be low and gas producing foods such as generous portions of raw vegetables cabbage beans rich pastries and charged drinks should be avoided The patient s tolerance for certain foods should also be taken into consideration Fresh milk is not well tolerated by all patients and should be omitted if abdominal distention or other distress occurs Tea and coffee in moderation are permissible Water and fruit juices need not be restricted because the patient will seldom ask for more than he needs The intake of sodium should be reduced to a minimum including the intake of ordinary salt sodium bicarbonate charged drinks or medication containing an appreciable amount of sodium

Constipation and Abdominal Distention

Patients are likely to become constipated while confined to bed Laxatives will be necessary but none need be used for the first two or three days unless the patient is uncomfortable A small daily enema of 500 cc of soap suds will prove most satisfactory especially during the first week Mild laxatives may then be used such as mineral oil 30 cc aromatic fluid extract of cascara 4 to 8 cc or milk of magnesia in similar dosage

Abdominal distention may be the result of inactivity improper diet constipation or other factors Distention can be avoided in many instances by following the dietetic suggestions mentioned before Involuntary swallowing of air may be reduced by drawing attention of the patient to his air swallowing when he gulps his food or when under emotional strain Flatulence may also be

relieved by a rectal tube, glycerine suppository, a mild laxative or a small enema containing soap suds

TREATMENT OF COMPLICATIONS AND SPECIAL SYMPTOMS

Treatment of Shock

Shock occurs frequently in acute myocardial infarction especially in the earlier stages of the attack It can be recognized by the collapsed veins of the neck, grayish pallor cold hands rapid pulse, prostration and fall in venous and arterial blood pressure The circulating blood volume may be reduced but this is not always the case in acute myocardial infarction if there is concomitant congestive heart failure [94] There is an important difference between ordinary shock and the form which occurs in acute myocardial infarction The heart in ordinary shock is undamaged and recovery may be expected if the circulating blood volume can be restored by rapid intravenous infusion of blood or plasma Shock in acute myocardial infarction on the other hand is associated with a severely damaged heart

I have recently employed desoxyephedrine hydrochloride in shock following acute or recurrent myocardial infarction The drug is injected intravenously in doses of 5 mg at intervals of five minutes until blood pressure rises well over 100 mm Hg or until a maximum of 15 mg has been used A sustaining depot of 10 mg may be injected intramuscularly at the same time and may be repeated in thirty minutes Successful results were obtained in three of four patients One patient developed supraventricular tachycardia which lasted several hours but caused no harm The pulse rate was not affected in the remaining patients nor were other untoward reactions noted

It is generally considered unwise to administer fluids intravenously in such instances of shock for fear of overloading the severely damaged heart I have administered as much as 1500 cc of plasma in shock following acute myocardial infarction without apparent ill effect on the heart or circulation No beneficial effects were observed, perhaps because the patients were already nearly moribund It is possible that earlier use perhaps of larger amounts, might have proved more beneficial Schwartz reports a patient who developed shock after an attack of acute myocardial infarction who received 2200 cc of plasma and blood within a

period of forty minutes This patient showed immediate improvement and recovered uneventfully [93] Additional measures which may prove of value are intramuscular injection of 0 5 gm of caffeine sodium benzoate or intravenous injection of 100 cc of 50 per cent dextrose solution every hour for three or four doses

Treatment of Congestive Heart Failure Following Acute Myocardial Infarction

The treatment of congestive heart failure during the early stages of acute myocardial infarction is the same as when it occurs under other circumstances It is believed by some that digitalis may favor rupture of the infarcted area that it favors thrombosis and may thus give rise to emboli or that it may induce ectopic beats or even ventricular fibrillation Such unfortunate accidents occur but it is far from proved that digitalis was the actual responsible factor There is good evidence that such accidents are just as frequent when digitalis is not used Congestive heart failure is a distinct threat to life and should be treated as energetically as when it occurs under other circumstances It is questionable judgment to permit hypothetical considerations to interfere with adequate treatment when the patient is in actual congestive heart failure The physician will do well to treat such congestive heart failure in accordance with the suggestions made on page 58

Treatment of Embolism Following Acute Myocardial Infarction

Embolism may occur at any time after an attack of coronary thrombosis but is most likely after the second week The most frequent sites for location of such emboli are the lungs and brain less often in the extremities at the bifurcation of the abdominal aorta and other regions The origin may be from a mural thrombus on the endocardial surface of the myocardial infarct or from bland thrombosis in the veins of the lower extremities

The immediate treatment consists of bed rest and subcutaneous injection of morphine sulfate 15 mg (¼ grain) for pain restlessness dyspnea or cough Papaverine hydrochloride 32 to 65 mg (½ to 1 grain) with atropine sulfate 1 mg (1/60 grain) are injected intravenously to relieve reflex spasm of the occluded vessel Further injections of 32 mg (½ grain) of papaverine may be given intramuscularly every four hours for the next two days

Pulmonary emboli may require administration of oxygen for

severe dyspnea or cyanosis in addition to the foregoing measures It may prove useful to inject 30,000 units of penicillin intramuscularly every three hours to prevent or combat secondary pneumonia Penicillin should be continued until the patient is free from fever for two days after which it may be reduced gradually and discontinued

Emboli to the extremities are treated by wrapping the part in warm blankets Other forms of local heat may produce burns It has been suggested that the affected extremity should not be elevated as this may interfere with the flow of blood beyond the obstruction Papaverine and atropine may be used as described Anticoagulants are employed to prevent recurrences and further thrombosis but they should be used only under strict control of the prothrombin time Embolectomy may be considered if the foregoing conservative measures fail to give adequate relief

The Treatment of Cardiac Arrhythmia and Paroxysmal Tachycardia During Acute Myocardial Infarction

Extrasystoles and short runs of auricular fibrillation are frequent in the first few weeks after acute myocardial infarction They are often transient and require no treatment unless they cause discomfort or embarrassment of the circulation

Extrasystoles paroxysmal tachycardia or auricular fibrillation which threaten to induce cardiac failure should be treated energetically Quinidine sulfate, 0 2 gm (3 grains) orally may be given every four hours provided this schedule proves successful within a day or two More resistant cases will require administration of 0 2 gm (3 grains) of quinidine every hour until the arrhythmia disappears or a maximum of ten doses are given that day Larger amounts may be necessary in very resistant cases but a total doasge of 3 gm should not be exceeded on any day Normal rhythm, when it is restored, may be maintained by 0 2 gm (3 grains) every four hours for two days and then four times daily for a week The number of doses may then be reduced gradually in accordance with the response of the patient Quinidine may be administered by a Levine tube passed into the stomach via the nose if the patient is unable to swallow or quinidine hydrochloride may be injected intramuscularly in the same dosage as used orally Acetyl beta methylcholine (mecholyl) may be employed (described on page 94) if quinidine fails Congestive heart

failure if present should be treated by rapid digitalization before quinidine is used A single oral dose of 0 6 gm (9 grains) of powdered digitalis or 1 2 mg of digitoxin may be given to improve the heart in such instances Subsequent dosage of digitalis is the same as described previously under treatment of congestive heart failure Quinidine may be administered as soon as there is definite relief of congestive heart failure

Treatment of Diabetes Mellitus During Acute Myocardial Infarction

Acute myocardial infarction exerts a profound effect on diabetes mellitus The patient becomes more resistant to insulin and the diabetic state becomes very labile The result is a marked increase in blood sugar with glycosuria and sometimes ketosis both of which are difficult to control This difficulty is increased further by the fact that great caution must be exercised not to injure the already damaged myocardium by too abrupt reduction of or too low a blood sugar level for the particular patient

Transient hyperglycemia and glycosuria may occur for a few days shortly after the onset of acute myocardial infarction in well controlled diabetics and even in nondiabetic patients This phenomenon is of little importance if hyperglycemia is moderate and no acetone is found in the urine No special treatment is necessary since both the hyperglycemia and glycosuria disappear spontaneously after several days

The development of *marked glycosuria and severe hyperglycemia* shortly after the onset of acute myocardial infarction *requires no change* in diabetic therapy from the kind the patient was getting before the attack *provided ketosis does not occur, i e no acetone is found in the urine* The hyperglycemia will generally return to former levels and the glycosuria will disappear or become much reduced in a few days to a week or two on the same diabetic management employed before the myocardial infarction occurred It may be necessary to cover the administration of insulin with adequate carbohydrate either orally or intravenously in the form of 10 per cent dextrose solution About 3 gm of dextrose for every unit of insulin may be used for this purpose

Diabetic patients whose diabetic state was not treated before the onset of myocardial infarction or those whose diabetic state becomes seriously unbalanced with no apparent return to a safe level after a week or ten days may be placed on a diet composed

of 70 gm of protein 70 gm of fat and 200 gm of carbohydrate The urinary bladder is emptied about one half hour before each meal Each of these pre meal specimens is tested for acetone and sugar and each specimen serves as a guide for the dosage of insulin which should be given before the meal which follows passage of this urine specimen A good working rule is to use 20 units of crystalline (regular) insulin if the sugar reaction is brick red, 15 units if orange and 10 units if yellow The aim in diabetic control of such patients should be a fasting blood sugar of 150 to 180 mg and/or a loss of 15 to 25 gm of sugar in the urine in twenty four hours Protamine zinc insulin may be substituted for the crystalline (regular) form when the diabetic state becomes stabilized i e , in about a week or ten days after the onset of the myocardial infarction The change may be made in the following manner Protamine zinc insulin in a dosage equal to one third of the entire daily dose of crystalline insulin used the previous day is added in the same syringe to crystalline (regular) insulin The amount of crystalline (regular) insulin thus used is also equal to one third of the total daily amount used the day before The mixture is injected thirty minutes before breakfast and pre meal urines are collected and tested as described previously A fasting blood sugar level or glycosuria in excess of those mentioned as the aim of treatment may be treated by gradually increasing the amount of insulin while keeping the diet constant The increase in insulin dosage in the morning may be made by adding 5 more units of protamine zinc insulin the next day An additional 5 units of crystalline (regular) insulin may be added the following day if the pre meal urines show the need for an increase Similar alternate increases may be made daily until satisfactory control is attained or regular insulin may be given before certain meals if necessary as indicated by the pre meal urine examinations The daily insulin requirement should be adjusted constantly during the entire stay in the hospital or until the patient becomes ambulatory Other methods including the use of globin insulin are also useful and are adequately described in textbooks on the treatment of diabetes

The *treatment of diabetes with severe ketosis* (acetonuria) shortly after acute myocardial infarction is difficult A solution of 10 per cent dextrose in distilled water may be given intravenously at the rate of 200 to 250 cc per hour up to a total of 1500 to

2000 cc There need be no fear of overloading the heart since patients in shock following acute myocardial infarction have received plasma and blood very rapidly in amounts up to 2500 cc with excellent results Similar amounts of the dextrose solution may be given orally by a Levine tube if necessary if the intravenous route is deemed inadvisable Crystalline (regular) insulin should be injected subcutaneously in a dosage of 15 to 20 units every two hours while the dextrose solution is being administered until only a trace of acetone is present in the urine collected every two hours Dextrose is necessary throughout the treatment in order to restore liver glycogen which is greatly depleted during acidosis The patient is then placed on a liquid diet for a day or two consisting of 6 equal feedings during the day Milk eggnog *thin cereal and orange juice may be used with a total carbohydrate* value of at least 200 gm the protein and fat content being of relatively minor importance The insulin dosage is determined by the 6 pre meal urine examinations as described previously The patient may be placed on a soft diet consisting of 3 main meals and an additional mid morning mid afternoon and late evening small feeding a day or two later Here too the diet may consist of 70 gm of protein 70 gm of fat and not less than 200 gm of carbohydrate Insulin is now given three times daily the dosage being determined by the urine specimens collected before the 3 main meals This regimen may be continued for several days until the patient can take an ordinary diet of the same food value as before with insulin adjustment to protamine zinc and crystalline insulin as described for patients with severe hyperglycemia

TREATMENT OF ANGINA PECTORIS

TREATMENT OF THE ATTACK

Most patients learn very early that immediate and complete arrest of physical activity or emotional excitement will soon result in disappearance of anginal pain It is not necessary to lie down in fact most patients prefer the upright position during the attack

Nitroglycerine (glyceryl trinitrate) tablets chewed and kept under the tongue, is effective and convenient *The smallest effective* dose should be used in order to prevent or reduce unpleasant side reactions such as throbbing headache or flushing of the face Doses of $\frac{1}{3}$ mg (1/200 grain) will generally suffice but larger

or smaller amounts should be used if necessary Neither tolerance nor addiction are likely even if used frequently over a long period of time The patient should carry a small supply of tablets preferably those prepared for hypodermic use, since these dissolve more rapidly The supply should be replenished every three or four months because nitroglycerine begins to deteriorate after a few months

Amyl nitrite is somewhat more potent but it has an unpleasant odor and may induce more severe side reactions than nitroglycerine Amyl nitrite is dispensed in small cloth covered glass ampules which are crushed in the hand or in a handkerchief and inhaled through the nose and mouth

It is important to indoctrinate the patient that neither nitroglycerine nor amyl nitrite is habit forming and that they afford *relief by improving coronary circulation It should be stressed* that they exert no narcotic action, that they do not "kill pain but that they relieve pain by improving blood flow to the heart muscle The patient will then understand why it is safe to use such nitrites as often as needed However, the patient should be warned that he should seek medical advice if two tablets fail to give relief since such persistent pain may be due to myocardial infarction

PREVENTION OF ANGINAL ATTACKS

Nitroglycerine and amyl nitrite will frequently prevent anginal pain if taken shortly before exertion emotion or other activity which is known to induce attacks Postprandial attacks may be avoided by taking nitroglycerine immediately after a meal

Further prophylactic treatment consists of avoidance of those habits which may precipitate anginal attacks Eradication of certain associated diseases which act as "trigger mechanisms is also important

Avoidance of habits which may precipitate attacks The patient should limit his exertion to bounds within his capacity and should avoid worry or excitement Sexual intercourse may induce anginal attacks and may prove very dangerous Meals should be small more frequent if necessary and the patient should rest for at least half an hour after eating Residence in a warm climate during cold or inclement weather may provide greater comfort but probably does not prolong life Patients should engage in a sedentary occupation or in one requiring only moderate exertion

Eradication of associated conditions which may act as trigger mechanisms in precipitating anginal attacks are also very important Obese patients should reduce weight, preferably by diet alone Reduction of weight should be gradual, not more than 1 or 2 pounds a week Patients are more likely to follow a diet which is not too rigorous and which avoids extreme hunger or weakness

Striking relief from anginal attacks may follow the cure of co existing thyrotoxicosis, anemia active peptic ulcer or so called spastic colitis Eradication of extrasystoles when possible may result in freedom from anginal attacks Biliary colic if due to gall stones should be treated by surgical procedures since this may have a very beneficial effect on the incidence of anginal attacks Patients with angina pectoris do not tolerate a low blood sugar level hence it is important not to overtreat diabetes It is better for such patients to spill some sugar in their urine than to run the risk of too low a blood sugar level by seeking perfection in diabetic management either by too strict a diet or too much insulin

Surgical procedures and nerve block are reserved for patients with intractable angina pectoris It must be remembered before resorting to such measures that an increase in frequency or severity of anginal attacks may presage an attack of coronary thrombosis Such patients may improve in a striking manner after being placed at absolute bed rest for about three weeks Moderate sedation nitroglycerine and the regimen generally followed in the treatment of actual coronary thrombosis, if followed for about three weeks provide striking relief and may prevent an attack of myocardial infarction

Patients who do not respond to such a regimen may benefit from nerve block Surgical interruption of the sensory pathways involved in angina pectoris has proved successful in many instances but is a very formidable procedure for such patients

Paravertebral injection of alcohol is fairly safe and has yielded good results in many instances [174] Complete failure has occurred in only 10 per cent in the hands of those who are experienced with the method Neither surgical interruption nor injection of alcohol alter the course of the disease, even when anginal pain is relieved completely Alcohol injections may be followed by sensory disturbances in the chest and upper extremities painful neuritis and other unpleasant effects which may persist for months

Other surgical procedures such as total thyroidectomy in the

or smaller amounts should be used if necessary Neither tolerance nor addiction are likely even if used frequently over a long period of time The patient should carry a small supply of tablets, preferably those prepared for hypodermic use, since these dissolve more rapidly The supply should be replenished every three or four months because nitroglycerine begins to deteriorate after a few months

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THE TREATMENT OF DISTURBANCES IN CARDIAC RATE AND RHYTHM

SINUS ARRHYTHMIA

Sinus arrhythmia occurs frequently in patients with normal hearts No treatment is necessary in such instances except assurance that this form of arrhythmia is not a sign of heart disease and that it will not lead to cardiac disability

Sinus arrhythmia may also be caused or become exaggerated by various toxic substances such as digitalis or quinidine This is not a sign of major toxicity and the drug should not be discontinued unless no longer necessary Cerebral arteriosclerosis basal meningitis increased intracranial pressure and various nervous or emotional disturbances may give rise to sinus arrhythmia Treatment should be directed to such underlying conditions since the sinus arrhythmia itself is harmless and will disappear when the causative factor is eliminated

SINUS TACHYCARDIA

There is no effective treatment which can be applied directly to sinus tachycardia The constitutional form which is present throughout the lifetime of the patient is harmless and requires no treatment other than assurance The same is true of sinus tachycardia due to nervous or emotional causes such as neurocirculatory asthenia

Sinus tachycardia may be caused by sensitivity to or excess of tobacco tea coffee alcohol and various drugs such as thyroid substance or ephedrine and its allies Tachycardia will usually disappear when these are discontinued although it may take several weeks before slowing is noted It is well to bear in mind that tachycardia may be the presenting complaint in thyrotoxicosis tuberculosis cardiac failure and other diseases and diligent search should be made to exclude such factors

absence of thyrotoxicosis or the attachment of various tissue grafts to the heart, are still in the experimental state and are not recommended

CORRECTION OF BASIC CORONARY INSUFFICIENCY

It is seldom possible to influence sclerosis of the coronary arteries or the effects produced by such anatomical changes Narrowing of the coronary ostia by syphilitic infiltration may sometimes be improved by careful antisyphilitic treatment The cautious use of iodides bismuth or mercury may prove beneficial Details of such treatment will be found in the chapter dealing with cardiovascular syphilis Penicillin if used for treatment of syphilis, may *precipitate a Herxheimer reaction which may prove very dangerous* Anginal pain which occurs in the presence of aortic valve insufficiency may be refractory to all treatment unless cardiac failure is a factor Digitalis and other measures designed to improve cardiac function may then prove beneficial or recourse to nerve block may become necessary

Xanthines have been used for many years to improve coronary circulation Their reputation is based chiefly on empiric grounds Xanthines dilate coronary vessels in pharmacologic, animal experiments but carefully controlled clinical observations on large numbers of patients do not corroborate the view that these drugs provide relief in man with any greater degree of frequency than placebos [143–147] Many xanthines cause digestive disturbances *Theobromine calcium salicylate in doses of 0 5 gm three times daily* is least likely to induce such unpleasant side effects and is probably not less efficacious than other so called coronary dilators Benefit can be derived from phenobarbital 15 mg (¼ grain) three times daily or a similar sedative either alone or in combination with a xanthine derivative

Patients with coronary disease including angina pectoris may *develop an anxiety neurosis* unless tact is employed in explaining their illness to them It is perhaps better to avoid the term angina pectoris and its serious implications *It will suffice to tell the* patient that his coronary arteries are thickened and that his attacks are due to insufficient blood flow The aims of treatment and reasons for various restrictions can then be fully discussed Relatives of the patient should of course be informed about the nature of the illness, including the possibility of sudden death

Sedatives such as 15 to 32 mg (¼ to ½ grain) of phenobarbital several times daily may be of value when nervous or emotional factors are responsible Oral administration of potassium acetate in doses of 5 to 10 gm is said to be of value in extrasystoles especially when due to digitalis [9]

PAROXYSMAL TACHYCARDIA

TREATMENT OF THE ATTACK

There are few therapeutic procedures which are as dramatic as the abrupt termination of an attack of paroxysmal tachycardia by some simple manual manipulation The physician will often be aided by the patient if the latter recollects that a particular manipulation proved successful in previous attacks for it is an interesting fact that the same manipulation will continue to prove successful in the same patient and yet will fail in others

Pressure on the carotid sinus is a simple and effective measure The patient should be in a supine position in bed Firm pressure is exerted by all 4 fingers with a massaging motion over the region of the carotid sinus This is located approximately at the anterior surface of the pulsating carotid artery at the anterior border of the sternocleido-mastoid muscle on a level with the thyroid cartilage Very firm pressure is exerted against the transverse processes of the cervical vertebrae on the right side for twenty or thirty seconds while listening to the heart sounds The left carotid sinus may be compressed later if pressure on the right side fails Pressure may be alternated on each side but both sides should not be compressed at the same time The carotid sinuses soon become refractory to pressure hence it is best to wait for some time after pressure has been applied two or three times It is important to remember that the carotid sinuses may become very sensitive after acute myocardial infarction and that serious results may follow compression in such circumstances

Pressure over the eyeball with the lids closed is sometimes effective Firm pressure for twenty or thirty seconds is made over the alternate eyeball The procedure is very uncomfortable and is not as reliable as carotid sinus pressure but may succeed occasionally when other measures fail

Many patients learn from experience that certain other procedures may prove successful Such measures consist of induction

SINUS BRADYCARDIA

We possess no direct treatment for sinus bradycardia The constitutional form requires no treatment other than assurance The forms associated with certain infections jaundice, increased intracranial pressure, starvation, myxedema or various drugs such as digitalis, *will disappear when the causative factor is eliminated* Sinus node standstill may occur with sinus bradycardia and may give rise to faintness if the duration of cardiac standstill is long enough Atropine sulfate ⅓ mg (1/200 grain) may be used orally three or four times daily since the underlying mechanism is often overactivity of the vagus

EXTRASYSTOLES (PREMATURE SYSTOLES)

The treatment of extrasystoles is frequently unsatisfactory unless *the underlying cause can be found and eradicated There is a very* large group of patients in whom there is no apparent cause for extrasystoles Such extrasystoles appear at an early age and persist throughout the lifetime of the patient They are generally harmless and require no treatment other than reassurance and avoidance of factors which are known to induce their more frequent occurrence Such factors are emotional tension fatigue worry and excessive use of tobacco alcohol, tea or coffee Various digestive disturbances may act in a similar manner notably over eating flatulence, constipation diarrhea or gall bladder disease

Extrasystoles may be due to toxic action of various drugs such as digitalis epinephrine or ephedrine and its allies Such extrasystoles will disappear when the causative drug is discontinued Extrasystoles are frequent in pregnancy and thyrotoxicosis but they are of no special significance and disappear after delivery or eradication of the thyrotoxicosis Extrasystoles which are due to organic heart disease are of more serious significance Relief of cardiac failure may cause such extrasystoles to become less frequent or to disappear, but more direct therapeutic measures may be necessary in such instances

The direct treatment of extrasystoles is unsatisfactory in many instances Quinidine sulfate in doses of 0 2 gm (3 grains) three or four times daily has been used either alone or in combination with strychnine sulfate, 1 mg (1/60 grain) and powdered digitalis 32 mg (½ grain) Quinidine is perhaps best used alone as outlined or at shorter intervals in recent acute myocardial infarction

who develop cardiac failure should be digitalized before intensive quinidine therapy is started This may be done by any of the methods described under congestive heart failure

It may be necessary, because of vomiting or for other reasons to use parenteral administration Quinine dihydrochloride, up to 0 5 gm, may be injected intravenously very slowly almost drop by drop until normal rhythm is restored The same amount may then be given intramuscularly at intervals of one or two hours until normal rhythm is restored if this has not been attained by the intravenous injection As much is 16 gm (240 grains) has been given in this manner in a period of forty eight hours [208] Quinidine dihydrochloride in the same dosage as given orally may be injected intramuscularly with safety It is reported that potassium chloride or acetate in doses of 1 to 2 gm orally combined with adequate quinidine and given every two to four hours, may prove of value if the latter alone is ineffective [09]

Freshly made syrup of ipecac has been used with success in paroxysmal tachycardia of supraventricular origin It is given in doses of 4 to 8 cc and may be repeated once or twice at intervals of an hour It may induce vomiting and other unpleasant symptoms but may be effective when other measures fail

DIGITALIS OR ITS ALLIES

These may be used if quinidine and pressure on the carotid sinus or eyeball and similar measures fail Digitalis is also indicated if cardiac failure begins to develop A single oral dose of 0 6 gm (9 grains) of the powdered leaf or 1 2 mg of a digitoxin preparation may be given and a third of these amounts may be administered again in six hours if necessary Strophanthin K 0 5 mg or an injectable preparation of digitalis equal in potency to 0 5 gm of the powdered leaf may be injected intravenously if oral administration is not practicable The same precautions should be taken as outlined in the discussion of digitalis in the chapter dealing with congestive heart failure An additional dose of one half the initial amount may be injected in four to six hours if necessary Digitalis is considered very dangerous in paroxysmal ventricular tachycardia and should not be used in such cases

Injection of alcohol into the right stellate ganglion has been used with success in paroxysmal tachycardia [10] The injection

or vomiting drinking ice water, holding the breath, lying in bed with the head low over the side or prolonged inspiration while keeping the glottis closed

Acetyl beta methylcholine (mecholyl) is frequently effective in paroxysmal tachycardia of supraventricular origin [96-98] Severe reactions may occur but these can be avoided by proper precautions The patient is placed in a reclining position and a constrictor is applied above the site of injection in order to control the rate of absorption A syringe containing 1 mg (1/60 grain) of atropine sulfate should be ready for immediate intravenous injection to combat untoward symptoms Acetyl beta methylcholine in doses of 20 mg for younger adults and 40 mg for those past middle age is then injected subcutaneously The constrictor is released intermittently for a moment or two for a total period of about fifteen minutes to permit fractional absorption Toxic symptoms such as flushing, nausea vomiting, asthma or collapse may appear alarming but can be controlled quickly by reapplying the constrictor and injecting the atropine in a vein of the other arm The constrictor may be removed in about fifteen minutes with little likelihood of recurrence of symptoms The carotid sinuses become more sensitive after acetyl beta methylcholine so that compression in a few minutes after injection may prove successful if it failed before

Quinidine sulfate orally is probably the most reliable drug for all forms of paroxysmal tachycardia A tablet or capsule containing 0 2 gm (3 grains) is administered every hour until normal rhythm is restored or for a maximum of 10 doses The first and second doses may be considered as test doses since absorption is rapid and attains a maximum in about two hours Sensitivity or toxicity will be detected at this time and the drug can be discontinued if necessary The more common untoward symptoms produced by quinidine include tinnitus deafness skin eruptions nausea vomiting diarrhea faintness collapse intraventricular block and a heart rate of 120 or more per minute Such symptoms if severe, require that quinidine be discontinued Attempts to restore normal rhythm may be made daily in accordance with the foregoing schedule but it is useless to persist for more than a week Normal rhythm when it is restored may be maintained with 0 2 gm (3 grains) every four hours night and day for two days and then four times daily for ten days to two weeks Patients

or distressing conditions in the abdomen Sedatives assurance and psychotherapy may prove beneficial when the patient is under emotional strain

AURICULAR FIBRILLATION

The treatment of auricular fibrillation will depend on the duration of the arrhythmia and on the condition of the myo cardium

Attempts to restore normal rhythm with quinidine will prove most successful in paroxysmal auricular fibrillation or in auricular fibrillation of recent origin Conversion of long standing auricular fibrillation to normal rhythm may prove successful but early re currence of the arrhythmia is frequent and the unpleasant sub jective symptoms associated with frequent change in rhythm may prove quite distressing to the patient

It is always a serious matter to use quinidine in advanced organic heart disease or in frank cardiac failure, for it is precisely in such patients that serious accidents including sudden death are most likely to occur It is thus apparent that restoration of normal rhythm with quinidine is best limited to the comparatively small group of patients in whom the auricular fibrillation is recent or is of the paroxysmal variety provided the myocardium is in fairly good condition and no frank cardiac failure is present

Patients with persistent auricular fibrillation of more than about three months duration or those in whom there is serious organic heart disease or cardiac failure are best treated by slowing the ventricular rate with digitalis Persistence of the auricular fibril lation when the ventricular rate is about 80 per minute will place little burden on the heart or circulation This procedure is safe and can be continued indefinitely and is thus the method of choice in the majority of patients with auricular fibrillation

GENERAL MEASURES

Patients undergoing treatment for auricular fibrillation should be at bed rest Search should be made for extracardiac causes especially for toxic nodular goiter with minimal signs of thyro toxicosis the so called masked hyperthyroidism Cardiac failure if present should first be eradicated by digitalis and other meas ures described under treatment of congestive heart failure

was followed by some pain in the shoulder and arm but the attack was terminated after other measures had failed and did not recur

PAROXYSMAL VENTRICULAR TACHYCARDIA

The treatment of paroxysmal ventricular tachycardia with quinidine differs somewhat from the methods used in other forms of paroxysmal tachycardia Pressure on the carotid sinus or eye ball is ineffective and digitalis is dangerous Treatment with quinidine sulfate is the method of choice It may be given orally in doses of 0 4 gm (6 grains) every hour until there is definite slowing of the heart rate, after which the dosage may be reduced to 0 2 gm (3 grains) every hour until normal rhythm is restored The occurrence of toxic symptoms will of course preclude further administration of quinidine The average total dose per day which is considered safe varies from 2 5 to 3 gm but larger amounts are justifiable in so dangerous a condition as paroxysmal ventricular tachycardia Levine has given as much as 1 5 gm five times a day without development of serious toxic manifestations [212] Maintenance doses of 0 2 to 0 4 gm (3 to 6 grains) may be given every four hours for a few days after normal rhythm is restored, after which the intervals may be lengthened gradually Quinidine should be continued for at least a week after normal rhythm is restored and preferably longer

PREVENTION OF ATTACKS OF PAROXYSMAL TACHYCARDIA

Prevention consists largely of avoiding factors which are known to precipitate attacks The most frequent are worry excitement fatigue overeating and abdominal distention There are patients who develop paroxysmal tachycardia from tea coffee, alcohol or tobacco either because they are sensitive to such substances or because they use them to excess Heart disease and thyrotoxicosis should be searched for and treated if found

There are many patients in whom no precipitating factors can be discovered No treatment is necessary if the attacks are short and if they occur at long intervals Quinidine sulfate, 0 2 gm (3 grains) may be given three or four times daily if the attacks occur every week or ten days or if they are prolonged or severe So called 'trigger mechanisms should be eradicated if found These consist of biliary colic active peptic ulcer or other painful

little or no digitalis during the preceding four or five days Smaller amounts possibly one half or less will be adequate to fully digitalize a patient if he is already under the influence of digitalis

Intravenous digitalization may be advisable in instances where time is a factor or where oral administration is impracticable as in severe cardiac failure or where the heart rate is very rapid Such patients may be given an intravenous injection of 0 5 mg of strophanthin K provided they received no digitalis for the preceding four or five days An additional dose of 0 25 mg may be given in six hours if necessary A digitalis preparation suitable for intravenous use may be administered if this is preferred to strophanthin The equivalent of 0 5 gm of the powdered leaf may be injected as an initial dose and half of this amount may be repeated in four hours if necessary Maintenance doses of 0 1 gm (1½ grains) orally or more may then be given once daily to keep the ventricular rate between 75 and 80 beats per minute

Auricular fibrillation due to thyrotoxicosis will frequently revert to normal rhythm spontaneously after thyroidectomy Iodine the thiouracil group and to a lesser degree digitalis may improve the arrhythmia before operation Quinidine usually fails before operation and should not be used at this stage but may be given about two weeks after thyroidectomy if auricular fibrillation persists

Auricular fibrillation which develops in the course of myocardial infarction may be transient Quinidine may be used as outlined before if the arrhythmia persists for more than a few hours or if the circulation becomes impaired Auricular fibrillation which develops in the course of certain febrile diseases is often self limited Direct treatment with quinidine or digitalis may become necessary when cardiac efficiency is impaired It is believed that digitalis is dangerous in active diphtheritic myocarditis hence it should not be used in such circumstances

AURICULAR FLUTTER

Short paroxysms occurring at long intervals require no special treatment of the attack other than bed rest and reassurance Attempts may be made to terminate attacks of auricular flutter by pressure over the carotid sinus or eyeball as described under treatment of paroxysmal tachycardia Failure to terminate attacks by such simple measures will require the use of digitalis or quinidine

METHOD OF RESTORING NORMAL RHYTHM WITH QUINIDINE

A tablet or capsule containing 0 2 gm (3 grains) of quinidine sulfate is administered orally every hour until normal rhythm is restored toxic manifestations are induced or a maximum of 10 such doses is given Sensitivity to quinidine and the symptoms of such intolerance are described in detail in the discussion of the pharmacologic properties of quinidine on page 35 Two or three *additional doses may be given in persistent cases if the quinidine* is well tolerated The method of restoring and maintaining normal rhythm is essentially the same as described on page 96 for the use of quinidine in paroxysmal tachycardia The same program may be repeated daily for about a week but other measures should then be used if normal rhythm has not been restored

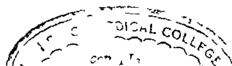
Serious accidents have been attributed to quinidine but these are not frequent if the patients are properly selected Embolism has occurred especially in patients with long standing auricular fibrillation or in those with serious heart disease The frequency of emboli is probably no greater with quinidine than with other forms of treatment [185] Patients have been observed in whom further emboli ceased to occur after normal rhythm was restored by quinidine Ventricular fibrillation has been reported but such occurrences are rare The most important untoward effects are depression of the myocardium various forms of heart block and fatal cardiac standstill

METHOD OF SLOWING THE VENTRICULAR RATE WITH DIGITALIS

This method is of little value when the ventricular rate is normal or slower It is of great value when the ventricular rate is above 90 per minute The powdered leaf in doses of 0 2 gm (3 grains) *is administered three times daily until* the rate at the apex is about 90 per minute The individual dose is then reduced by *one half until the apical rate* approaches about 80 per minute after which maintenance doses of 0 1 gm ($1\frac{1}{2}$ grains) or more is given once daily indefinitely *Digitoxin is preferred by many* physicians because of its complete absorption An initial dose of 0 9 mg may be given with an additional 0 3 mg in six hours if necessary in order to digitalize the patient Maintenance doses of 0 1 or 0 2 mg or more may then be given daily in accordance with requirements These methods of digitalizing the patient with digitalis or digitoxin are applicable only if the patient has received

VENTRICULAR FIBRILLATION

Large doses of quinidine orally or by intramuscular in
offer the only hope in this extremely serious form of arrh
when it occurs in paroxysmal form The method of adm
tion is the same as in paroxysmal tachycardia Sustained ven
fibrillation is not compatible with life



DIGITALIS

Unlike auricular fibrillation, auricular flutter may be converted to normal sinus rhythm by administration of adequate digitalis Digitalis is thus the drug of choice, particularly if signs of cardiac failure develop The powdered leaf in doses of 0 2 gm (3 grains) may be given three times daily until the ventricular rate approaches normal or toxic symptoms develop Auricular fibrillation may develop during such digitalization but digitalis should not be discontinued at this point Digitalis should be continued until the ventricular rate approaches normal regardless of the type of *auricular mechanism A normal* ventricular rate may *then result* from restoration of normal sinus rhythm in the auricles or to high grade auriculoventricular block with the auricles still in a *state of flutter or fibrillation Slowing of the ventricles to a normal* range with any of these mechanisms is a satisfactory therapeutic result A normal ventricular rate should be maintained by daily rations of 0 1 gm (1½ grains) or more of digitalis daily There are some patients in whom normal sinus rhythm is restored if digitalis is discontinued after the drug has converted auricular flutter to auricular fibrillation with slow ventricular rate

Intravenous injection of digitalis or its allies may be used in urgent cases in severe cardiac failure or where oral administration is impracticable The methods and precautions are the same as those described under treatment of auricular fibrillation

QUINIDINE

Quinidine sulfate may be used in the same manner as *in* paroxysmal tachycardia if digitalis fails The ventricular rate may at times be increased temporarily after quinidine This is due to *slowing of the rate of auricular oscillations* by quinidine with consequent improvement of auriculoventricular conduction It will generally be necessary to use maintenance doses of quinidine for ten to fourteen days after normal rhythm is restored in order to prevent recurrence There are patients who will respond to no form of treatment including digitalis and quinidine, and who then may have normal rhythm restored spontaneously after weeks or months of no treatment There is not much to be done in such instances except to be on the alert for evidences of cardiac failure and to treat it energetically as described previously under cardiac failure

DISTURBANCES OF CONDUCTION

SINO AURICULAR BLOCK

Sino auricular block often is self limited and requires no special treatment unless the cardiac pause is sufficiently prolonged to cause faintness or syncope Such patients may be put to bed and 0 65 mg (1/100 grain) of atropine sulfate may be given orally three times daily Digitalis or quinidine if responsible for the block should be discontinued although they may be used with caution if severe cardiac failure or serious arrhythmia still threaten the patient

AURICULOVENTRICULAR BLOCK

Incomplete auriculoventricular block either with prolonged P R interval or with dropped ventricular beat causes little or no circulatory embarrassment and requires no special therapy Digitalis or quinidine if responsible for the block should be discontinued although their use may be continued cautiously if serious cardiac failure or threatening arrhythmia persist Incomplete heart block which is not due to digitalis will not be made worse by that drug even if used in full therapeutic doses hence there need be no hesitancy in the use of digitalis in such instances if cardiac failure is present

Incomplete auriculoventricular block may be caused by syphilitic involvement of the heart although this is rare Cautious antisyphilitic therapy may be employed as described in the chapter on syphilis of the heart and aorta Heart block is not rare in diphtheria and may sometimes be improved by intravenous administration of dextrose solution as described under treatment of diphtheritic myocarditis

Patients with *complete heart block* should limit their efforts to bounds within their capacity Removal of the underlying cause should be attempted if possible There is no reliable direct treat

cc every four hours, day and night for four or five days after which the frequency of injections can be decreased gradually in accordance with the condition of the patient The total amount of epinephrine used each day is not excessive, palpitation and other side effects are minimal or absent and a rise in blood pressure seldom occurs even in the presence of hypertension Undue sensitivity *to epinephrine may be overcome by barbiturates shortly* before the injection of epinephrine is given Atropine barium chloride and ephedrine or its allies when administered orally have proved disappointing Digitalis is definitely contraindicated unless the danger from congestive heart failure is very great since it may exaggerate the degree of block Digitalis may be resumed if necessary after the tendency to Adams Stokes syndrome has passed

Attacks of Adams Stokes syndrome due to paroxysms of rapid tachycardia or ventricular fibrillation require an entirely different method of treatment Epinephrine and digitalis may prove dangerous and are contraindicated in this form of Adams Stokes syndrome Quinidine is the drug of choice and it should be administered as in paroxysmal tachycardia (See page 94)

ment which can be used in complete heartblock Barium chloride ephedrine and similar substances have usually proved disappointing Digitalis, even in full doses may be used if cardiac failure is present since the block cannot be made worse and systolic contraction may be strengthened

INTRAVENTRICULAR OR BUNDLE BRANCH BLOCK

Here too no direct treatment is known which is useful in this type of heart block The underlying cause if ascertained should be treated or eradicated This form of heart block is no contraindication to digitalis or other measures which are used in cardiac failure

ADAMS STOKES SYNDROME

It is important to ascertain whether this syndrome is due to cardiac standstill to very rapid paroxysmal tachycardia or to attacks of ventricular fibrillation Electrocardiographic studies should be made before therapy is begun if such a distinction cannot be made from the history and physical examination

The immediate treatment of short attacks due to cardiac standstill consists of artificial respiration and intramuscular injection of 0 5 cc of a 1 1000 aqueous solution of epinephrine More prolonged attacks due to cardiac standstill require heroic measures including artificial respiration and intracardiac injection of epinephrine Epinephrine in amounts of 0 25 to 0 5 cc of 1 1000 aqueous solution is used A needle about 3 inches long is inserted into the fourth left intercostal space about ½ inch from the sternal border The needle is pushed to a depth of about 2 inches before injecting the epinephrine It makes no difference whether the needle is in the myocardium or in the ventricular or auricular cavity Shorter attacks of cardiac standstill lasting ten or fifteen seconds especially if they recur at frequent intervals should be treated by subcutaneous injection of epinephrin at regular intervals I have had good results with the following method The patient is placed at absolute bed rest and an initial dose of 0 5 cc is injected subcutaneously This is followed by injections of 0 25 cc every hour for 6 doses and then every four hours for the remainder of the day and night It may be necessary to repeat the series of hourly injections every day until cardiac standstill no longer occurs The effects may then be maintained by injection of 0 25

INFECTIOUS DISEASES OF THE HEART AND AORTA

CARDIO AORTIC SYPHILIS

There are three principles upon which modern treatment of cardio aortic syphilis is based These are improvement of the unctional state of the cardiovascular apparatus arrest of the syphilitic inflammatory process and avoidance of harm by over zealous antisyphilitic treatment

It is seldom wise or possible to eradicate completely the syphilitic infection once the cardiovascular system is involved No more should be attempted than the arrest of syphilitic inflammatory processes in such patients unless cardiovascular involvement is minimal

Adequate continuous treatment early in the course of syphilitic infection or during its clinically latent phase will almost always prevent syphilitic involvement of the cardiovascular system [13] [215] Treatment will be much more difficult and restoration of anatomical integrity impossible once such involvement has occurred

All patients except those with minimal involvement of the cardiovascular system should be at bed rest during the early phases of treatment [13] Congestive heart failure no matter how slight should be treated in a routine manner as outlined on page 53 until maximum improvement of dyspnea edema and congestion of the lungs and liver has been attained Cardiac failure incident to syphilis frequently is highly resistant to digitalis and larger amounts may be necessary to achieve satisfactory results [14] Congestion of the lungs and liver as well as edema will respond well to mercurial diuretics Such diuretics should be used during congestive failure without fear of untoward consequences since this form of mercury is dissociated with difficulty in the body and nearly all of the metal is excreted in twenty four hours

Syphilitic aortitis which is uncomplicated by aneurysm insufficiency of the aortic valve or by congestive heart failure may be treated more energetically Potassium iodide 1 to 2 gm, is administered orally three times daily for three months During the same time an insoluble bismuth salt is injected in doses of 0 025 gm of a preparation averaging 50 to 60 per cent metallic bismuth These injections are given at intervals of five days for 6 doses after which the amount is gradually increased to 0 2 gm if well tolerated Doses of 0 2 gm are then given at intervals of a week for a total course of three months Arsenicals may then be started without an intervening rest period Arsenical treatment is begun with neoarsphenamine 0 05 gm or mapharsen 0 01 gm once a week These are increased by 0 05 gm of neoarsphenamine or 0 01 gm of mapharsen each week to a maximum of 0 3 gm of the former or 0 03 gm of the latter each week for a total course lasting three months Courses of bismuth with iodide and of arsenicals each of three months duration are alternated without intervening rest periods for a total of not less than two years The patient is then observed periodically for the remainder of his life time and a three month course of bismuth followed by a course of arsenicals for a similar period are administered every year

Patients with syphilitic aortic valve insufficiency or aneurysm should be treated less intensively if cardiac failure cannot be relieved completely No antisyphilitic therapy should be used in old age poor general health or in associated hypertensive cardio renal disease Only iodides and bismuth may be employed if cardiac failure cannot be completely relieved Patients with aortic valve involvement or with aneurysm who are not in cardiac failure or in whom cardiac failure is relieved completely may be treated by a series of 80 successive intramuscular injections of bismuth arsphenamine sulphonate (bismarsen) without interruption after the preliminary administration of an initial course of plain bismuth for three months The initial dosage is 0 025 gm twice a week The individual dose is increased gradually to 0 1 gm in the course of 10 or 12 injections The amount is then increased more rapidly until a dose of 0 2 gm is reached The latter dosage may be administered every five or seven days for the remainder of the series Bismarsen is well tolerated seldom causes reactions and is a fairly dependable antisyphilitic remedy

Antisyphilitic therapy is begun only after maximum improvement of congestive heart failure has been attained *It is imperative* to avoid nitritoid reactions, the Jarisch Herxheimer phenomenon and the so called therapeutic paradox The nitritoid reaction begins shortly after or during injection of almost any arsenical *The reaction consists of sudden intense flushing of the face, dyspnea,* cough and anxiety There may also be edema of the face and loss of consciousness The immediate treatment consists of subcutaneous or intramuscular injection of 0 5 to 1 cc of 1 1000 solution of epinephrin Nitritoid reactions may be avoided in many instances by using small doses of the less toxic arsenicals when such drugs are necessary The Jarisch Herxheimer reaction occurs within a few hours to a day or more after the first injection of the arsenical It consists of fever malaise and flaring up of syphilitic lesions all over the body There may be abrupt edema and swelling of the syphilitic involvement at the ostia of the coronary arteries with sudden closure of the vessels or aortic aneurysms may dilate suddenly or rupture Such reactions may have serious consequences and may cause death but they can usually be prevented by using bismuth for eight to twelve weeks before small doses of arsenicals are administered [216] *The therapeutic paradox may also cause very* serious consequences It consists of a period of initial improvement followed by abrupt and almost intractable congestive heart failure This reaction may also be prevented by an initial period of treat*ment with bismuth for two to three months before arsenical* treatment with small doses is begun

The kind of antisyphilitic treatment to be used will depend on the absence or presence of irreducible congestive heart failure and on *the location and type of syphilitic involvement of the* cardiovascular system The following plan of treatment has been moulded largely by the excellent discussion by J E Moore on treatment of cardio aortic syphilis [21]

Patients in congestive heart failure which cannot be improved appreciably should be maintained on standard treatment for congestive failure as outlined on page 53 Potassium iodide may be administered in doses of 0 5 gm three times daily and this amount may be increased gradually to 2 gm per dose *if it is well tolerated* Mercurial diuretics may be administered as often as every third day This will aid in controlling congestion and edema and may furnish a small amount of mercury as an antisyphilitic

must also be prepared to deal with cardiac failure should this arise

Bed Rest

Rest in bed with a minimum of activity is very important during active rheumatic infection Adults present no difficulties but children will frequently continue some degree of activity even when confined to bed One must do the best possible in such circumstances using sedation at night for sleep if necessary There is no set rule concerning the length of time of bed rest but it is common practice to keep the patient in bed until three weeks have passed during which all evidences of rheumatic activity have disappeared There is no single criterion of rheumatic activity but the general nutrition of the patient should be improved and the temperature sedimentation rate white blood count and electrocardiogram should all be normal before it is safe to assume that the rheumatic process has become inactivated Persistence of joint pains presence of rheumatic nodules or a pulse rate over 90 per minute are reliable signs that the rheumatic infection is still active and that further bed rest is necessary All of the foregoing manifestations of activity should be observed after salicylates and similar medicaments have been discontinued for about five days in order to exclude the possibility that therapy is masking the true condition of the patient

Patients who are confined to bed for many weeks should keep occupied with educational and vocational activities This will aid the morale of the patient and will in some measure maintain the progress of the child s education Older patients may be taught some sedentary vocation so that they will continue to be useful members of society All such activities during the period of bed rest and convalescence must be controlled strictly in accordance with the capacities of the patient Undue fatigue, rise in heart rate or fever or exacerbation of the evidences of rheumatic activity mentioned previously are indications that the effort has been too great for the patient and that such activities should be reduced or discontinued

Nursing care is important The skin should be kept dry and well powdered to prevent irritation from profuse sweating The patient should assume a position in bed which provides the most comfort The diet should be as appetizing and nutritious as possi

for such patients A course of plain bismuth followed by one of bismarsen, each of three months duration, might well be given every year for the remainder of the patient's life Mapharsen may be used intravenously in the dosage previously suggested if the aneurysm or aortic valve involvement is of minimal degree Here too a course of bismuth for three months should precede the arsenical for a similar period of time alternately without interruption for at least two years

The treatment of patients with cardiovascular syphilis who also have anginal pain is beset with difficulties It is best to begin with bismuth and iodides for three months as outlined and then to proceed very cautiously with bismarsen, provided this is well tolerated It is probably best not to use arsenicals intravenously in such patients

Cardiovascular syphilis is frequently associated with syphilis of the central nervous system The cardiovascular involvement is usually the more dangerous and should be treated before therapy of the central nervous system is undertaken Tryparsamide in doses of 1 to 3 gm may be used with safety since it is well tolerated in cardiovascular syphilis although it has no therapeutic effect on the latter condition

Penicillin has been used successfully in the treatment of various forms of syphilis Jarisch Herxheimer reactions have not been rare when the cardiovascular system is involved It is advisable that patients receive preparatory treatment for about three months with bismuth and iodides before penicillin is administered It may be wise to use much smaller doses of penicillin perhaps 1000 units as an initial amount with an increase of 500 units at each succeeding dose The intramuscular injections could be given every three hours with a maximum total daily dose of about *150 000 units until a total of about 4 000 000 units are given* The routine use of penicillin in cardiovascular syphilis is not advised however until much more information is accumulated as to dosage safety and efficacy of this form of treatment

ACTIVE RHEUMATIC CARDITIS

The treatment of rheumatic carditis is essentially the same as that of rheumatic fever in general All smouldering rheumatic infection must be eliminated since any residue may reactivate the carditis In addition to inactivation of rheumatic infection one

Acetylsalicylic acid (aspirin) may be used in similar dosage if sodium salicylate is not well tolerated Acetylsalicylic acid is not as soluble as sodium salicylate and passes into the bowel before it can irritate the stomach Amidopyrine may be used but it some times induces leukopenia or agranulocytosis Iron in the form of pills of ferrous sulfate in doses of about 1 gm daily may prove very useful in the presence of anemia Sulfonamides and penicillin are without value in active rheumatic infection [n 1 3] Vaccines serums foreign protein therapy and roentgen therapy have no striking beneficial effects

Cardiac Failure

The treatment of cardiac failure during active rheumatic carditis is essentially the same as for other forms of congestive heart failure and is discussed in detail on page 53 Digitalis is useful but will be found less effective in the presence of rheumatic activity in the heart Larger amounts will be needed and children may require doses almost as large as those given to adults Heart block if due to rheumatic infection is no contraindication to the use of digitalis in regular dosage Cardiac arrhythmia as well as heart block often disappears spontaneously and requires no special treatment except when the circulation is embarrassed Digitalis or quinidine may be used if tachycardia is due to auricular fibril lation or flutter The method of administration and dosage are de scribed on pages 98 100 Theobromine calcium salicylate in doses of 1 gm three times daily or other xanthines have been recom mended as diuretics Better results will be obtained by the use of mercurial diuretics in the presence of dyspnea edema or con gestion of the lungs or liver Cardiac failure during active rheu matic carditis may resist all treatment until rheumatic activity subsides after which the heart failure may subside spontaneously

Precordial pain and distress caused by pericarditis may be re lieved by application of an ice bag to the precordium and the use of codeine or morphine Large pericardial effusions have dis appeared after administration of massive doses of salicylates about 15 gm a day Pericardial paracentesis is seldom necessary in rheumatic infection unless compression of the heart is serious The results are almost always disappointing as there is great practical difficulty in distinguishing the signs of cardiac enlarge ment from those due to pericardial effusion

ble It is well to urge the patient to drink as much water and fruit juices as possible in order to compensate for the loss incident to fever and sweating

Salicylates

Salicylates lower fever and relieve *pain and discomfort in the* articular tissues but they do not shorten the course of the disease or affect the causative factor of rheumatic fever There are some who believe that salicylates affect rheumatic carditis favorably[16] [17] It is the consensus of opinion however, that salicylates do not *prevent cardiac involvement or affect the heart appreciably once* it becomes involved[218, 219, 220]

It will be useful to administer salicylates in active rheumatic carditis for the antipyretic effects and for the possible benefit they may otherwise exert Sodium salicylate is the preparation *of choice It should be given in large initial doses with equal amounts* of sodium bicarbonate Adults may be given 1 gm of sodium salicylate every hour for 8 to 10 doses unless toxic symptoms develop These are epigastric distress nausea, vomiting, headache tinnitus deafness and vertigo Visual and mental disturbances and manifestations of acidosis are *less frequent Salicylates should* be discontinued for two or three days if toxic symptoms develop after which smaller doses, 0 5 to 0 75 gm may be given hourly for 8 or 10 doses Large initial doses in the absence of toxic manifestations, may be continued until maximum improvement is attained after which the amount may be reduced *to 1 gm four times* daily Salicylates in the foregoing dosage should be continued until rheumatic infection has been apparently inactivated for about ten days before further reducing the daily dosage The amount administered should be reduced gradually over a period of about a week *before the drug is finally discontinued*

Rectal administration is useful if salicylates cannot be tolerated orally A retention enema consisting of 10 gm of sodium salicylate in 150 cc of thin starch water may be given daily after a cleansing enema has emptied the bowel Rectal administration may be *followed by the same toxic manifestations as after oral use Vomit*ing may occur as a result of action on the nervous system Salicylates may be injected intravenously but this route is unnecessary and has no special advantages since salicylates are absorbed rapidly from the gastro intestinal tract including the rectum[225]

patients usually remain free from such reactions if no toxic effects are noted in the first two or three weeks [4] It is necessary to see the patient every week at first and to determine his hemoglobin and white blood count at each visit Weekly visits are made for two months after which the interval is lengthened to once a month for the duration of prophylactic treatment

There is little evidence that removal of tonsils or eradication of other foci of infection play an important part in preventing an initial attack of rheumatic fever or recurrences I have seen several patients with inactive rheumatic heart disease who developed subacute bacterial endocarditis following the extraction of an infected tooth Tonsillectomy or eradication of foci of infection should not be attempted until rheumatic endocarditis or heart disease has remained inactive for several months

The question of a change to a warm climate frequently comes up for consideration Such a move should not be contemplated unless the patient can live permanently in such a climate The assumption of undue financial burdens the matter of good schooling or a suitable vocation are additional considerations which should be given serious thought Resorts or places which are frequented by transients should be avoided in order to reduce the risk of coming in contact with infectious diseases

Other preventive measures such as the prophylactic use of penicillin salicylates vaccines and serums have not as yet been proved of value

SUBACUTE BACTERIAL ENDOCARDITIS

The use of penicillin for successful eradication of active infection in subacute bacterial endocarditis was first reported in 1944 by Loewe Rosenblatt Green and Russell [30] and a few months later by Dawson and Hobby [231] These observations were soon confirmed by other workers in a larger number of patients Sufficient time has now elapsed to warrant the conclusion that the use of large doses of penicillin for an adequate length of time will result in eradication of infection and healing of inflammatory processes in from 70 to 80 per cent of all patients with subacute bacterial endocarditis

The earlier methods consisted of administration of large amounts of penicillin by continuous intravenous infusion together with the use of anticoagulants to prevent further accretion of thrombotic

Patients with rheumatic heart disease in whom infection has become inactivated may lead a normal life provided their activities are kept within the bounds of their cardiac capacity Such patients should choose a sedentary occupation and should engage in normal activities if possible Competitive sports strenuous exercise and exposure to inclement weather should be avoided Congestive heart failure when it develops should be treated as outlined on page 53

Prophylaxis

No specific measure is available for prevention of initial or recurrent attacks of rheumatic fever It is very likely that there will be none until the cause of rheumatic fever is known It will be useful in the meantime to maintain the patient s nutrition at a high level and to avoid chilling, inclement weather, and exposure to persons with contagious disease particularly sore throat and upper respiratory infections

Very encouraging results have been obtained by the use of prolonged continuous daily administration of sulfonamides as a prophylactic measure against *recurrent* attacks of rheumatic infection [5, 6, 22, 28, 29] Observation of large numbers of patients with suitable controls over periods up to ten years has shown that recurrence of rheumatic activity may be reduced to one fifth or less The method consists of giving sulfanilamide or sulfadiazine in doses of 0 5 gm three times daily throughout the year for a period of at least five years in the case of adults and in children until the patient reaches the age of twenty one Sulfonamide prophylaxis is initiated after rheumatic activity has subsided but before the patient leaves the hospital The patient must be asymptomatic and afebrile and the white blood count must be normal although it is unnecessary to wait for a normal sedimentation rate before starting sulfonamides It is necessary, of course, that the foregoing criteria of inactivity be obtained after salicylates have been discontinued for at least a week Toxic reactions are mild and comparatively rare especially with sulfadiazine The most common are nausea vomiting skin eruptions, mild fever moderate anemia and leukopenia It is unnecessary to discontinue the sulfonamide unless the toxic reaction persists or becomes more severe Toxic reactions when they occur, are most likely to appear during the first few weeks after sulfonamides are started but

The method developed by us and the one we still employ in the majority of our patients consists of intramuscular injection of penicillin every hour day and night. It is based upon the principle that the concentration of penicillin in the serum begins to

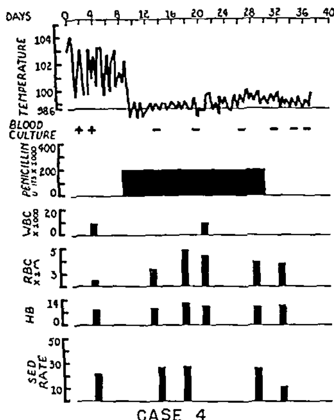


Fig. 7.—Example of rapid and permanent cure with penicillin. A 51 year-old woman with a history of rheumatic fever. An abscessed tooth was extracted two days before admission but no prophylactic treatment was employed. Three blood cultures were positive for Streptococcus viridans. There was a presystolic murmur at the apex and a palpable spleen. Penicillin 8,500 units was injected intramuscularly every hour day and night for twenty-one days. There has been no recurrence during the subsequent period of observation which is nearly three and one half years.

fall sharply in the second hour after an intramuscular injection.[5]

[38] We have found that hourly intermittent intramuscular injections of penicillin will maintain a high and effective concentration of penicillin in the blood at all times. More recent studies in our

material on the surface of the vegetations It soon became *evident* in our own work and in the experience of others that anticoagulants were not necessary [3, 233, 34, 3, 236] Experimental proof that anticoagulants are unnecessary was recently furnished by Nathanson and Liebhold who showed that penicillin penetrates such vegetations with ease [37] It also became apparent that interrupted intramuscular injection of penicillin was as efficacious as continuous intravenous infusion provided the same daily dosage was used for the same length of time



Fig 6 —Healed stage of subacute bacterial endocarditis after treatment with *penicillin Section of stump of aortic cusp showing no evidence of active inflammation or indications of bacterial activity*

Most clinicians now use interrupted intramuscular injection of penicillin It was formerly necessary, when very resistant organisms were encountered to use larger amounts of penicillin by intravenous infusion since not enough old penicillin could be dissolved in 1 or 2 cc of solvent the usual volume for intramuscular injection Crystalline penicillin which is now available is much more soluble It is very likely that enough penicillin can now be injected intramuscularly to meet all requirements The frequency of injection varies but the total daily dosage and the duration of treatment *depend* on the sensitivity of the causative organism to penicillin and the clinical response to therapy

rate may remain moderately accelerated for several weeks after other signs of active infection have disappeared to become normal spontaneously after a short time [34, 35] Patients who harbor more resistant organisms may require treatment for several months

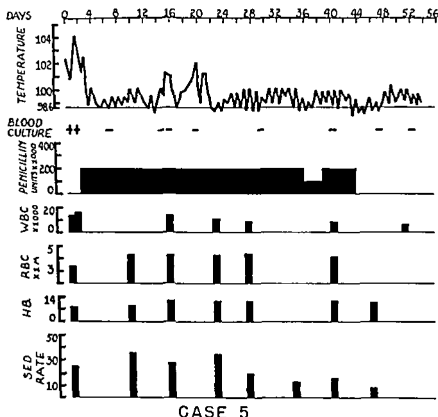


Fig 8 — A 19 year old girl with a history of congenital heart disease and congenital syphilis Chills and fever began one week after extraction of an abscessed tooth "Machinery" murmur over pulmonic area and a diastolic murmur at the junction of the left third rib and sternum Three blood cultures were positive for Streptococcus viridans The patient received 8300 units of penicillin intramuscularly every hour day and night for six weeks No evidence of acute infection since treatment nearly three and a half years ago Operative repair of the patent ductus arteriosus not contemplated because of the associated aortic valve incompetence

before active infection is finally eradicated No patient should be discharged from the hospital immediately after penicillin is discontinued All patients should be watched closely for two more weeks after all therapy is discontinued during which time further

patients have shown that a good average blood level of penicillin may be maintained by using larger individual doses at longer intervals We are now using doses of 50 000 units every two hours with good results This method permits the use of the same total daily dose with injections at intervals of two hours, i e, 12 instead of 24 injections in twenty four hours The total daily dosage is determined from the *in vitro* sensitivity of the causative organism to penicillin We aim to maintain a penicillin blood level from five to ten times the *in vitro* sensitivity figure but it is wise from a practical standpoint to use not less than *600 000 units every twenty four hours* The organism obtained from blood culture is tested for sensitivity to penicillin by the serial dilution method, using a standard strain of staphylococcus aureus of known sensitivity as a control Strains of streptococci which respond to less than 0 06 Oxford Unit will generally react favorably to 600 000 units of penicillin in twenty four hours More resistant strains will usually require more the actual dosage being determined by clinical trial with increasing amounts We have given as much as *3 000 000 units in twenty four hours in one case and 6 000 000* units in another with success in patients with very resistant organisms

The total twenty four hour requirement of penicillin is dissolved in slightly more than 24 cc of solvent and 1 cc is injected deeply in the buttocks and elsewhere every hour day and night Continuous intravenous infusion is used if the individual dosage required is too great to be dissolved in 1 cc of fluid the usual volume for intramuscular injection Continuous intramuscular drip has been used successfully [34] [41] There is no real advantage with this method since the patient soon becomes accustomed to hourly injections, even during sleep and absorption is apparently more certain

The duration of treatment should be from six to eight weeks, preferably the latter but therapy should not be discontinued until there is reasonable evidence that infection has been overcome permanently It may be assumed that active infection is eradicated when general nutrition is definitely improved when at least 3 consecutive blood cultures remain sterile and when the temperature and white blood count have become normal It is preferable that the sedimentation rate also return to normal but this is not necessary since we and others have observed that the sedimentation

the course [30 33 4] Regular penicillin administration should be continued on the day before during and after extraction if penicillin is already discontinued and the sockets should be packed with gauze saturated in penicillin solution, employing 5 000 units per cubic centimeter of solvent We have used para amino hippuric acid successfully to raise the concentration of penicillin in the blood where the organism was very resistant and the patient seemed to grow progressively worse in spite of very large doses of penicillin We employed the method of Beyer Flippin Verwey and Woodward which retains penicillin in the blood by greatly reducing renal elimination of penicillin [39] The method consists of simultaneous continuous intravenous infusion of large doses of penicillin in a 6 per cent sodium para amino hippurate solution Acute toxicity of sodium para amino hippurate is low and practically no symptoms are encountered when the rate of infusion is adjusted to 80 mg per kilogram per hour Caronamide has recently been suggested in doses of 2 gm orally every four hours to increase the concentration of penicillin in the plasma Priest and McGee have recently reported success with streptomycin in patients with streptococci highly resistant to penicillin and suggest that streptomycin might be of value when the causative agent is a gram negative bacillus insensitive to penicillin [40] They used 500 000 units (0 5 gm) per day but state that the dose must be adjusted in accordance with the needs of the patient

Congestive heart failure may develop in from 20 to 25 per cent of patients after recovery from active infection [3 43] It is probably due to myocardial damage and to increased deformity of heart valves after healing by scar tissue The degree of failure will depend on the extent of damage but treatment is the same as outlined for congestive heart failure on page 53

THE HEART IN INFECTIOUS DISEASES

The cardiovascular system may become involved in many forms of infectious disease It is important however to distinguish between actual cardiac involvement and peripheral circulatory collapse Peripheral circulatory collapse is initiated by peripheral vascular dilatation and later by decreased circulating blood volume with inadequate venous return to the heart Treatment in such instances is directed chiefly to restoration of the blood volume by intravenous infusion of blood plasma or other fluids

blood cultures and pertinent laboratory work should be studied to make certain that infection is actually eradicated It is a source of satisfaction that recurrence is rare in patients who are treated adequately especially if there is no evidence of activity for three or four weeks after treatment is discontinued

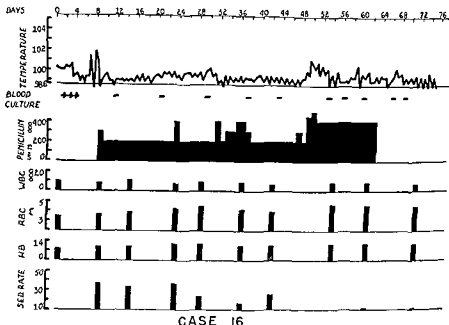


Fig 9—A 21 year old woman with a history of rheumatic pancarditis and congestive heart failure at the age of eight Slight to moderate cardiac failure since then Ill for three weeks with evidences of subacute bacterial endocarditis and pregnancy of about three months duration Three blood cultures positive for Streptococcus viridans She received 8300 to 16 600 units of penicillin intramuscularly every hour for fifty six days Abdominal hysterectomy was performed on the forty first day of treatment because it was felt that the patient's cardiac condition not the infection would not permit successful pregnancy The patient made an uneventful recovery and has remained well up to the present almost three years after treatment

Supplementary treatment is useful and generally is necessary A high caloric high vitamin diet should be used Blood transfusions of citrated blood or packed red cells should be given at the beginning of treatment if anemia is present which is usually the case Bed rest is desirable as long as fever persists Additional symptomatic treatment such as hypnotics sedatives iron laxatives etc should be used as indicated It is believed that infected teeth should be removed during treatment in order to shorten

CONGENITAL MALFORMATIONS OF THE HEART AND GREAT VESSELS

Significant advances have been made in the treatment of certain forms of congenital malformations of the heart and great vessels Infection superimposed on congenital defects can be eradicated by penicillin or other antibiotics and various malformations may now be cured or relieved by surgical treatment

PATENT DUCTUS ARTERIOSUS

Patent ductus arteriosus was formerly considered a comparatively innocuous congenital malformation Careful studies show that 80 per cent of such patients die as a result of this condition at an average age of thirty five in other words their life expectancy was shortened considerably About 60 per cent of the deaths were due to cardiac failure and 40 per cent to subacute bacterial endarteritis and endocarditis [245]

Successful ligation of a patent ductus arteriosus was performed by R E Gross and subsequently by a number of other surgeons The indications for operation according to Gross[246] are

1 Retardation of physical development This is best appraised after the patient reaches six years of age or more

2 Cardiac failure or embarrassment of the circulation either in the past or at the time of examination This includes appreciable enlargement of the heart or undue increase in heart rate after moderate exercise

3 Orthopnea

4 Subacute bacterial endarteritis of the patent ductus arteriosus was added later as a further indication [47]

5 Patients with patent ductus arteriosus of significant dynamic magnitude in whom none of the foregoing indications for operation are present are now advised to undergo surgery in order to lengthen life and to prevent the various complications which frequently occur

Cardiac involvement, on the other hand often requires little more therapy than treatment directed to the underlying, systemic infectious disease Cardiac involvement which develops in the course of acute infectious disease is often transient, lasting a few weeks and leaving no permanent damage in later years More severe involvement of the heart must be treated by bed rest antibiotics and symptomatic treatment including therapy of cardiac failure if it develops It is well to remember that digitalis and its allies are frequently much less effective in the presence of active infection or inflammation of the myocardium

Myocardial involvement in diphtheria is a much more serious disease although here too, no permanent damage results in patients who survive the acute stage Treatment consists of strict bed rest until all signs of myocardial involvement including electrocardiographic changes, have disappeared Sitting up or getting out of bed during the active phase of diphtheritic myocarditis may be followed by sudden death Adequate antitoxin early in the course of diphtheria, is the best prophylactic measure against subsequent myocarditis but it is of little value after the toxin of diphtheria damages the heart Stimulants such as epinephrin or caffeine are of little value and may do harm The same is true of digitalis and its allies Beneficial effects have been reported after intravenous or intramuscular injection of 100 to 200 cc of 10 per cent dextrose solution [244] Improvement is often only temporary but the injection may be repeated as often as necessary until the patient is on the road to recovery

recovery with return of systolic blood pressure to normal in the upper extremities and appearance of normal pulsations in the lower limbs The best age for operation is between sixteen and twenty, i e, before the proximal aorta becomes dilated and too thin The technic has now been perfected so that there is a comparatively low operative mortality in the hands of those experienced in such operative procedures

OTHER MALFORMATIONS OF THE AORTA AND LARGER VESSELS

Congenital double aortic arch may compress the trachea or oesophagus and cause dyspnea or dysphagia Surgical division of one of the aortic arches is feasible and is followed by relief of symptoms An anomalous right subclavian artery may interfere with nursing This artery may be divided with good results Circulation to the arm is maintained adequately by collateral vessels after such an operation [0]

PULMONARY STENOSIS WITH INADEQUATE CIRCULATION TO THE LUNGS

Pulmonary stenosis with inadequate circulation to the lungs may be relieved by surgery if associated with the tetralogy of Fallot pulmonary atresia with or without dextroposition of the aorta and with or without defective development of the right ventricle a truncus arteriosus with bronchial arteries and a single ventricle with a rudimentary outlet chamber in which the pulmonary artery is small in size [1] The operation consists essentially of anastomosing a branch of the aorta and one of the pulmonary arteries i e the creation of an arteriovenous fistula in order to re aerate some of the blood in the aorta before distribution to the periphery The best age for operation is in children over two years of age so that the vessels are large enough to manipulate The operation is difficult but relief of cyanosis dyspnea and fatigability is very rapid and oxygen saturation is increased greatly Excellent results were obtained in nearly three fourths of the patients The operative mortality has been about 14 per cent Another operation has been devised recently which consists of a direct anastamosis between the aorta and adjoining pulmonary artery [5] Here too an arteriovenous communication is made

The initial operation consisted of mere ligation of the patent ductus but it was not always possible to attain complete and permanent obliteration of the vessel Ligation was then combined with wrapping of cellophane around the vessel to stimulate regional formation of scar tissue and further constriction The latest and best method consists of completely dividing the patent ductus arteriosus The operative mortality in experienced hands is very low All patients show marked gain in weight and physical development Cardiac failure disappears and subacute bacterial endarteritis is completely eradicated

The best results are obtained when only uncomplicated cases of patent ductus arteriosus are submitted to operation It is very questionable whether operation should be advised when other cardiac abnormalities, either congenital or acquired, coexist The operation should not be performed when the patent ductus arteriosus acts as a compensatory mechanism for other associated congenital defects

Operation has been successful in eradication of nonrheumatic infection of the patent ductus It has been our practice to treat such patients with penicillin in the manner described for subacute bacterial endocarditis Infection can be arrested in a few weeks and the patient then becomes a better surgical risk because of greatly improved general health and healing of the local processes in the ductus Operation is then advised in order to prevent recurrence

COARCTATION OF THE AORTA

Coarctation of the aorta may be well tolerated and may be compatible with a long and active life Serious complications may develop in others which can lead to incapacity and death Hypertension above the coarctation rupture of the aorta and infection with the streptococcus viridans may occur at any time, hence surgical correction of the constriction is justified in such patients

Experiments on animals showed that a segment of the aorta could be resected successfully [248] This was followed by successful resection of the coarcted aortic segment in humans [249] A fairly large number of patients have since been operated by this method As much as 1½ inches of the narrowed segment of the aorta is resected with subsequent suture of the two ends of the aorta No bleeding and no stenosis followed and the patients made a good

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DISEASES OF THE PERICARDIUM

ACUTE FIBRINOUS PERICARDITIS

The basic principles in treatment include eradication of the underlying cause when possible bed rest and such symptomatic therapy as may be necessary Salicylates may be given in rheumatic pericarditis as outlined under treatment of rheumatic carditis General hygienic measures are indicated in tuberculous pericarditis thyroid substance in myxedema appropriate vitamin therapy in *vitamin deficiency* and *antibiotics* such as *penicillin* when pericarditis is of bacterial origin

Bed rest is necessary in all instances until symptoms and manifestations of infections or inflammatory activity are no longer present The most comfortable position in bed will generally be a semi sitting posture The patient should remain in bed until the temperature heart rate white blood count sedimentation rate and electrocardiogram have all returned to normal and have remained so for about two weeks after all medication has been discontinued

Discomfort and pain will usually disappear when inflammation subsides Precordial pain may be controlled by the application of an ice bag and by oral administration of codeine 15 mg (¼ grain) or sodium salicylate 0 6 gm (10 grains) several times daily Morphine or its allies may be used if the foregoing measures prove inadequate

PERICARDITIS WITH EFFUSION

The same general therapeutic measures which were outlined for acute fibrinous pericarditis are useful in pericarditis with effusion

Paracentesis is indicated if cardiac tamponade develops i e if pericardial effusion causes severe dyspnea orthopnea engorgement of the veins of the neck congestion of the liver or rapid drop in blood pressure The technic of pericardial paracentesis

for the same purpose as in the operation described above Equally good results have been obtained with both types of operation but neither should be attempted unless the surgeon is experienced in this field of surgery It is to be remembered that such operations are merely palliative in the sense that they increase comfort and probably prolong life *They are not curative and the ultimate outcome after several years remains to be determined*

NONRHEUMATIC INFECTION OF CONGENITAL MALFORMATIONS OF THE HEART AND GREAT VESSELS

Such congenital malformations are subject to infection particularly by the streptococcus viridans The method of treatment is the same as described for subacute bacterial endocarditis The results are equally good but surgical repair should be attempted after infection has subsided if the lesion is one which can be treated successfully by surgery This will prevent recurrence of the infection as well as other complications incident to the malformation itself

Other forms of congenital heart disease must still be treated symptomatically Such patients like those with chronic rheumatic heart disease, are often less resistant to infection than normal children hence they should be protected from exposure to various infectious diseases and inclement weather Nutrition should be maintained at a high level Cyanosis and dyspnea when due to interference with oxygen exchange in the lungs should be treated by administration of oxygen and cardiac failure will require the measures described under congestive heart failure

The needle is pushed through the previously anesthetized area in the skin and a small amount of procaine is deposited in the deeper tissue The needle is then pushed in further in short thrusts with infiltration of the path as the needle approaches and enters the pericardial cavity The plunger of the syringe should be with drawn slightly after each thrust to determine whether fluid has been reached

The average depth to which the needle is inserted is about 3 or 4 cm in any of the routes except those near the sternum Fluid may not be obtained immediately upon entering the pericardial sac It may be necessary to tilt the needle in various directions to insert it a bit farther or to withdraw it for a short distance A stylet may be inserted in the needle to make certain that the lumen is not obstructed by a flake of fibrin It is wise to tilt the needle so that it lies parallel to the surface of the heart once the fluid is *reached This will reduce trauma to the surface of the heart* as it strikes against the point of the needle at each systole

The removal of even small amounts of fluid may be followed by striking relief No attempt should be made to remove all of the fluid and under no circumstances should more than 500 to 700 cc be aspirated at any one sitting Paracentesis may be per formed as often as necessary in order to provide symptomatic relief It has been recommended that removal of pericardial fluid in tuberculous pericarditis be followed by introduction of about 150 cc of air into the pericardial sac There is no agreement that any useful purpose is served by such treatment and there are reports that disagreeable symptoms may result

PURULENT PERICARDITIS

This condition may now be treated successfully by aspiration of the fluid and instillation within the pericardial sac of 10 000 to 20 000 units of penicillin in 10 to 30 cc of physiologic solution of saline [4, 255] Intramuscular injection of 30 000 units of penic illin every three hours day and night should be used at the same time until the condition is under control No reactions were noted and both the aspiration and instillation of penicillin may be repeated as often as necessary Surgical drainage with further local and general treatment with penicillin or other antibiotics will be necessary as in other abscess cavities if conservative meas ures prove inadequate

is described in the following section on the treatment of tuberculous pericarditis

It is frequently very difficult in the presence of active rheumatic heart disease to decide which signs and symptoms are due to the effusion and which to cardiac enlargement It is well to remember that pericardial paracentesis is seldom if every necessary in active rheumatic heart disease even if pericardial effusion is present Such effusions are generally much smaller than is estimated from clinical evidence Resorption takes place readily as the inflammatory process subsides especially after the use of salicylates Boas and Ellenberg reported rapid resorption of rheumatic pericardial effusion after oral administration of 10 to 14 gm of salicylates daily [53]

TUBERCULOUS PERICARDITIS

The fibrinous variety requires the same general measures employed in the treatment of tuberculosis elsewhere in the body Tuberculous pericarditis with effusion is treated in the same manner but paracentesis may be necessary if cardiac tamponade develops Surgical treatment other than aspiration is disappointing and may prove disastrous

Pericardial paracentesis is performed with a needle about 3 inches (7 5 cm) long and about 1 mm in diameter The patient is supported on a back rest in a semi sitting position after receiving a subcutaneous injection of 15 mg (¼ grain) of morphine or one of its allies The site of puncture is cleaned and sterilized in the usual manner and the skin is anesthetized by infiltration with a 1 per cent procaine solution Several sites are available but the one chosen most frequently is in the left fifth interspace about 1 or 1½ cm inside the left border of cardiac dullness or left border of the roentgen shadow of the heart A point within the fourth or fifth interspace near either the left or right border of the sternum may also be used provided it is within the area of cardiac dullness The epigastric route has the advantage that it drains the more dependent portions of the pericardial sac The needle is inserted at the junction of the left costal arch and sternum and is then directed upward and backward at an angle of about 30 or 35 degrees for a distance of about 4 cm or until fluid can be aspirated It is well to attach a large syringe containing 10 or more cc of the procaine solution to the needle before puncture is attempted

Surgeons skilled in this type of operation obtain complete cure in about 50 per cent definite improvement in about 25 per cent and failure or death in the remaining 25 per cent Such results must be considered quite satisfactory in view of the gravity of the illness and the futility of all other forms of treatment

Medical treatment alone may be necessary if surgical management is not available or if it is contraindicated The chief measures are bed rest, restriction of salt and fluid intake mercurial diuretics and drainage of effusions in the abdomen and chest by paracentesis Digitalis is of little or no value since the fundamental disturbance is mechanical interference with venous return to the heart rather than to inherent myocardial failure The patient may improve from time to time on such management but the course is progressively down hill with death after a prolonged period of invalidism unless surgical treatment can be instituted

CHRONIC ADHESIVE PERICARDITIS

Adhesions between the pericardium and other structures including the chest wall were formerly believed to cause myocardial exhaustion and cardiac failure Experimental and clinical evidence shows that the strain of constant tugging against such adhesions does not play as important a part in cardiac failure as was formerly believed unless there is coexisting myocardial or valvular disease The decisive factor even in such instances is the myocardial and valvular disease rather than the adhesive pericarditis Operations designed to free such adhesions or to make the chest wall less rigid are believed to fall short of what pericardial surgery can offer [1] The treatment of such patients is primarily medical and consists of the measures described in the therapy of congestive heart failure but Brauer s cardiolysis operation may be considered if conservative measures fail

CHRONIC CONSTRICTIVE PERICARDITIS

Chronic constrictive pericarditis is a condition in which the heart becomes encased in a fibrosed thickened pericardium Like all scar tissue the thick nonelastic pericardium shrinks thus compressing the heart so that it cannot accommodate itself to normal diastolic filling The result is engorgement of all veins proximal to the heart with congestion of organs and tissues drained by such veins Cardiac output is reduced as a result of diminished venous return to the heart and to a lesser degree by interference with systolic contraction [5] Adhesions to other structures may or may not be present but these are of minor significance Interestingly enough it is quite rare for other important forms of heart disease to be present in patients with constrictive pericarditis

Surgical decortication of the thick nonelastic pericardium is the most satisfactory form of treatment The prospects of complete cure are good and recurrence of symptoms is rare The technic of this operation is described in the excellent reports by Churchill [58] Beck [256] Blalock and Burwell [59] and by Harrington [60] Heuer and Stewart believe that operative mortality can be reduced below the average 25 per cent by careful preoperative preparation [61] These authors plan a long and very careful preoperative regimen with the result that they could report eighteen operated patients without a single death

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THE HEART IN HYPERTENSION

Cardiac complications are frequent in hypertension The more frequent are congestive heart failure angina pectoris and myocardial infarction Treatment of these conditions is discussed elsewhere here only the therapy of hypertension will be described

ASYMPTOMATIC HYPERTENSION

Treatment of hypertension is still unsatisfactory *Nervous or emotional strain* is an important factor in hypertension especially in persons with a familial history of elevated blood pressure All sources of worry or anxiety should be eliminated if possible especially concern about the patient's own hypertension The patient should be assured and encouraged and it should be pointed out that a long and active life is possible even when blood pressure has persisted for years at high levels It will be well to emphasize that it is the condition of the arteries rather than the height of the blood pressure which is important Frequent determinations of blood pressure should be avoided and efforts should be made to prevent the patient from becoming fixed to the sphygmomanometer Regular hours moderation in work and exercise and a calm state of mind will do much to dispel the nervous symptoms which are often attributed wrongly to hypertension The foregoing measures are frequently sufficient for the average patient with asymptomatic hypertension

HYPERTENSION WITH CARDIAC SYMPTOMS

Bed rest will result in temporary reduction of hypertension in many instances and may ward off impending cardiac failure or other distress The best results are seen in the earlier stages of essential hypertension when marked fluctuations are still present The maximum drop is generally observed during the first week after which the blood pressure remains more or less stationary Unfortunately the blood pressure begins to rise again shortly

drug The dose may be increased if the blood pressure does not fall and the blood level is less than 6 mg per 100 cc provided no toxic symptoms develop They report sustained improvement in about 47 per cent of their patients The dose must be varied and the blood level watched during the entire course of treatment which is for the lifetime of the patient since hypertension returns when the drug is discontinued Thiocyanates can cause severe toxic reactions and even death but blood pressure is sometimes lowered when other measures fail The margin of safety is narrow and death may occur when the blood level is under 12 mg per 100 cc , the so called safe maximum Toxic symptoms occur in a considerable number of patients even when blood levels are within the safe range It is problematical whether the somewhat better results obtained with thiocyanates in lowering blood pressure justify their use in view of their toxicity and the close supervision under which they must be given

DIET

Diet has been an important element in the treatment of hypertension Reduction of weight in obese patients is important and can be achieved by use of a well balanced 1200 calorie diet The loss in weight will be gradual intense hunger and weakness will be avoided and the patient will be re educated in his eating habits Thyroid substance is to be used with caution and only when necessary Violent exercise hot baths steam cabinets and similar measures are dangerou The best results will be obtained by severe restriction of salt and other dietary elements

It has been known for many years that hypertension and edema can be relieved by reduction in intake of salt and particularly of sodium Kempner has recently popularized severe restriction of salt protein and fat and reports excellent results with such a diet in hypertension [11] He has shown by clinical and laboratory studies that such a diet does not result in depletion of blood proteins and hemoglobin and he has demonstrated that nitrogen balance is maintained in spite of severe restriction of proteins This would seem to refute the contention that his results are due to starvation of the patient

Kempner reports significant reduction in hypertension in more than 60 per cent of patients and the reduction persists as long as the patient is maintained on the diet There is also loss of edema

after the patient leaves his bed. Bed rest is of value chiefly when hypertension causes severe *headache, vertigo and other symptoms* including impending cardiac complications.

Drugs do not induce a sustained drop in blood pressure unless such medication is continued indefinitely. Most drugs lose their effect after a few days. Little or no benefit can be expected from drugs in hypertension associated with nephritis or in malignant nephrosclerosis. The best results will be obtained in the earlier stages of essential hypertension.

Sedatives, by relieving nervous tension, may be of value, especially in essential hypertension. Phenobarbital in doses of 15 to 30 mg. ($\frac{1}{4}$ to $\frac{1}{2}$ grain) three times daily or bromides in doses of 0.65 to 1 gm. (10 to 15 grains) two or three times a day may prove useful. It will be wise to alternate a period of barbiturate for a week *with a period of bromides for a similar length of time in* order to prevent development of tolerance for the former or bromism with the latter.

Nitrites may reduce blood pressure in hypertension but this is by no means the rule. Nitroglycerine produces only a transient fall in pressure and is not suitable where sustained lowering is desired. The preparations employed for more sustained reduction in blood pressure are sodium nitrite in doses of 65 mg. (1 grain), mannitol hexanitrate 15 to 30 mg. ($\frac{1}{4}$ to $\frac{1}{2}$ grain) or erythrol tetranitrate 15 to 30 mg. ($\frac{1}{4}$ to $\frac{1}{2}$ grain) three times daily. All *three exert about the same clinical effect, which is usually not* very striking. Erythrol tetranitrate frequently causes severe headache. All nitrites result in tolerance with loss of effect in a few days but this tolerance disappears after the drugs are discontinued for two or three weeks. A further disadvantage is that development of tolerance to any one establishes cross tolerance to all other members of the nitrite group.[188]

Thiocyanates or sulfocyanates have again been advocated for hypertension when symptoms occur. Barker and his co-workers suggest that potassium thiocyanate be administered in doses of *0.3 gm. (5 grains) daily and that the dose be adjusted in accordance* with the blood level and clinical effects.[205] They state that a blood level between 8 to 12 mg. per 100 cc. is ideal and that this level should not be exceeded. A rapid drop in blood pressure during the first two weeks or the development of toxic symptoms requires reduction in dosage or complete discontinuance of the

obtained excellent results with this method of treatment with the patient at work provided he cooperated faithfully

The diet consists essentially of 200 to 300 gm of any kind of rice as much sugar as desired and about 1000 cc of fruit juice daily The rice is served at all meals and may be boiled or steamed

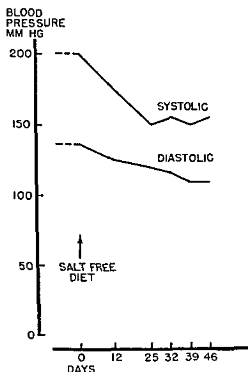


Fig 11 —The effect of treatment of hypertension in a 57 year old man by means of a salt free diet The hypertension had been present for thirty years intermittent at first but persistent for the last six years Thiocyanates and other methods of treatment were ineffective The blood pressure on initial examination July 25 1947 was 200/136 mm Hg The patient was placed July 25th on the regimen just described and with the results shown above Additions to the diet as outlined in the legend of Figure 10 were begun on August 20th The patient feels well and keeps at his work without difficulty

Ordinary white rice may be added slowly to boiling water and allowed to boil for twenty minutes more It is then drained in a collander washed with hot water and served or it may be steamed for twenty minutes more before serving Washing with hot water is omitted if wet rice is preferred Sugar oranges pineapple or apples either fresh or canned, may be added for variety

improvement in retinopathy and in the electrocardiogram, and cardiac enlargement is reduced This regimen is very useful in persistent hypertension particularly when cardiac failure with or without edema or congestion develops It will prove of value when

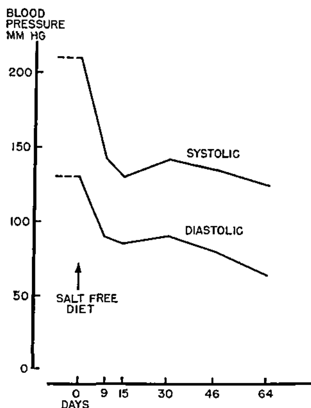


Fig 10 — The effect of treatment of hypertension in a 53 year old woman by means of a salt free diet The patient had had hypertension for at least four years with headache tinnitus nervousness and nocturia The average sustained systolic blood pressure was well over 190 mm Hg The blood pressure on initial examination was 210/130 mm Hg She was placed on the foregoing regimen on April 1 1947 with the results illustrated in this Figure Eggs fish chicken vegetables and salt free bread were added on April 15th The patient remained ambulatory during the entire course of treatment with maintenance of the blood pressure at normal levels for the first time in four years

the patient is prone to attacks of pulmonary edema or where edema or congestion are resistant to diuretics and other forms of treatment The difficulty lies in maintaining so monotonous a diet Many patients refuse to follow it after a variable length of time unless they are under strict supervision in a hospital I have

different operation [63] Their results were approximately the same although their mortality rate was 3 6 per cent

These results are encouraging and may be improved in the future Not all patients with hypertension should be submitted to operation Asymptomatic hypertension should be treated by conservative measures unless the blood pressure remains very high for more than a year or definite changes begin to occur in the heart, cerebral vessels kidneys electrocardiogram or heart Low salt diet and other measures should be tried before patients are selected for operation since the reported results are at least as good as with surgery and no harm can be done Selection of patients for operation should be made on the basis of probability of a good result as described by Smithwick and Peet [6, 63]

The total daily diet will thus furnish about 2000 calories and will consist of about 450 gm of carbohydrate, 20 gm of protein 5 gm of fat 0 2 gm of sodium and about 0 15 gm of chloride All fresh fruits and fruit juices are allowed except nuts, dates and avocados Dried or canned fruits are permitted provided only sugar has been added Tomato juice and other vegetable juices water and especially salt or other forms of sodium are not permitted

Patients will usually lose considerable weight, especially during the first two or three weeks but most of this is due to loss of water Larger portions of food may be served if the patient becomes weak or very hungry It will be useful to administer 0 6 to 1 gm of ferrous sulfate and the following as a supplement to the strict diet as outlined vitamin A, 5 000 units vitamin D 1,000 units thiamine chloride 5 mg riboflavin, 5 mg niacinamide, 25 mg and calcium pantothenate 2 mg

Additions may be made to the diet after satisfactory results have been attained but these should be added one at a time in order to determine the patient's tolerance and response Non leguminous vegetables small portions of potatoes lean beef chicken fish or an egg a day may thus be added A rise in blood pressure, recurrence of edema or reappearance of any other unfavorable sign will require immediate return to the original rice and fruit diet

SURGICAL TREATMENT OF HYPERTENSION

The only operation which actually cures hypertension is removal of a pheochromocytoma when this tumor is the cause of high blood pressure Removal of adrenal tumors or unilateral nephrectomy in disease of one kidney has proved disappointing

Great interest has been aroused by the good palliative results obtained by supra and infradiaphragmatic splanchnic resection although no permanent cures have as yet been reported Smithwick observed a large group of patients for several years after operation More than one half showed significant improvement in blood pressure eye grounds, electocardiogram, cardiac and renal function and general well being [6] The operative mortality was 2 2 per cent Postural hypotension and other disagreeable symptoms followed operation but disappeared gradually after several months Peet and his co workers reported on a somewhat

THE HEART IN ENDOCRINE AND METABOLIC DISORDERS

THE HEART IN MYXEDEMA

The goal in treatment should be maximum freedom from cardiac symptoms with the smallest possible amount of thyroid substance which will accomplish this purpose This rather than a normal basal metabolic reading should be the mark at which to aim

The usual measures employed in ordinary congestive heart failure will not greatly affect disturbances in cardiac function due to myxedema Digitalis is badly tolerated and opiates are very dangerous in such patients

Cautious oral administration of a standard U S P preparation of thyroid substance is the most important single element in treatment [264] It is better to work up gradually to the required dosage than to run the risk of untoward symptoms by using larger amounts at the beginning of treatment Commercial preparations of thyroid are not all of the same potency per unit of weight Hence one should familiarize oneself with the effects of a chosen manufacturer and use that product exclusively The average initial dose of thyroid substance is 100 mg (1½ grains) once daily preferably in the morning This is continued until maximum improvement is attained or symptoms of overdosage develop The amount may be increased gradually if there is no appreciable improvement after two or three weeks Thyroid substance should be discontinued if manifestations of overdosage occur such as precordial pain palpitation or cramp like pains in the extremities No further thyroid should be given until all such symptoms disappear, after which one half of the previous dose may be given daily until maximum improvement is noted The effects should then be maintained by somewhat smaller amounts daily for the rest of the patient s lifetime

The ideal basal metabolic rate in the treatment of myxedema

continued until the basal metabolic rate levels off and maximum general improvement of the patient has been attained

Direct treatment of the cardiac manifestations may also be necessary Congestive heart failure should be treated by bed rest digitalis mercurial diuretics restriction of salt intake and the other measures described in the chapter on treatment of congestive heart failure The efficacy of digitalis is reduced in the presence of thyrotoxicosis hence larger doses may be necessary Auricular fibrillation is not a contraindication to surgery and may disappear spontaneously after operation No special preoperative treatment of auricular fibrillation is necessary other than digitalis if cardiac failure is present Quinidine should not be used preoperatively as it seldom proves useful and may induce untoward symptoms Quinidine may be given about ten days postoperatively if auricular fibrillation or other arrhythmia persists

Patients who fail to improve with ordinary preparatory treatment including the use of iodine or those whose cardiac failure is too severe to withstand surgery may be treated by conservative measures Prolonged remissions and even cures have been reported following the use of thiouracil propylthiouracil and radioactive iodine Cardiac symptoms may be relieved and sinus rhythm may replace auricular fibrillation when such conservative measures result in eradication of thyrotoxicosis

Thiouracil and propylthiouracil act by preventing synthesis of thyroid hormone [26] The symptoms of thyrotoxicosis may persist for two or more weeks after these drugs are administered due to the fact that the normal storage depots of thyroid hormone are not yet exhausted Thyrotoxicosis ceases when all thyroid hormone in these depots is exhausted and no further synthesis takes place while the patient is under the influence of the drug

Thiouracil is administered orally since it is absorbed rapidly from the gastro intestinal tract Williams and Clute suggest that doses of 0 2 gm be given three times daily for two weeks and then twice daily until the basal metabolic rate becomes normal The dose is then reduced to 0 1 gm twice daily for the next two or three months and then once daily indefinitely [66] Prolonged remissions may be obtained if thiouracil is administered over a long period of time [67] It is the consensus of opinion that thiouracil is not an ideal drug for prolonged use and that it should be em

is −5 to −10 per cent but this is subordinate to freedom from symptoms as an objective in treatment It is not always possible to relieve all symptoms completely, hence, it may be necessary to compromise with partial relief if somewhat larger doses of *thyroid induce untoward effects*

Thyroid substance, when given in proper amounts will result in improvement of cardiac function decrease in size of the heart return of the electrocardiogram toward normal, and will induce diuresis Other therapeutic measures will not be necessary unless some factor other than myxedema is responsible for residual cardiac dysfunction The measures discussed in treatment of con gestive heart failure may be used in such patients after maximum benefit has been attained with thyroid substance

THE HEART IN THYROTOXICOSIS

There is considerable evidence that thyrotoxicosis does not sufficiently injure the previously healthy heart to induce cardiac failure Cardiac failure when it does occur, is believed to be due to the additive effect of the burden of thyrotoxicosis to pre existing cardiac damage It follows that eradication of thyrotoxicosis in such circumstances may play an important part in the relief of heart failure by removing one of the two important causative factors

Subtotal thyroidectomy is still the most effective method for permanent eradication of thyrotoxicosis The risk of operation can be diminished greatly by proper preparatory treatment and *patients may leave the hospital in a few days after operation* The so called thyrocardiac is rarely unable to withstand operation Even severe cardiac failure may not prove to be a strict contra indication after careful preparation and if the operation is per *formed as a hemithyroidectomy in two stages*

Preoperative preparation of thyrotoxic patients with cardiac disturbances consists of the usual measures such as rest in bed sedation and a high caloric diet rich in carbohydrates with the addition of *vitamin B* Extra *feedings of candy ice cream* and other carbohydrates between meals are useful in raising storage of glycogen in the body Lugol s solution (compound solution of iodine) 10 drops in a glass of milk three times daily or some other preparation *of iodine is indispensable* These measures are

continued until the basal metabolic rate levels off and maximum general improvement of the patient has been attained

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ployed chiefly as a preparatory measure before operation when iodine fails in this respect It is less effective in nodular toxic goiter and in patients who were using iodine shortly before thiouracil is begun Relapse follows in several months after the drug is discontinued but the chief objection to thiouracil is the fact that untoward reactions occur in about 13 per cent These unfavorable reactions include granulopenia agranulocytosis edema urticaria, and other skin eruptions, fever, allergic arthritis, vomiting abdominal pain, diarrhea or enlargement of the salivary glands Patients receiving thiouracil should be examined every week and should have blood studies for the first eight weeks and then at intervals of a month Thiouracil should be discontinued if granulopenia, arganulocytosis or high fever occurs It has been noted that reactions are more likely to occur if the patient received thiouracil or sulfonamides on previous occasions

Propylthiouracil has been suggested recently as a more potent drug to suppress thyrotoxicosis [268] It has the advantage that untoward reactions are much less frequent even when thiouracil is not well tolerated The average dose for suppression of thyrotoxicosis is 50 to 75 mg daily with maintenance doses of 25 to 50 mg daily thereafter Larger doses, from 200 to 300 mg daily, have been employed more recently with better results and no untoward reactions It is very possible that propylthiouracil may be satisfactory as a substitute for surgery if cardiac involvement is too severe to permit operation

Radioactive iodine has produced apparent cure of thyrotoxicosis in a small number of patients [269, 270] This method of treatment is still in the experimental stage but may prove of great value when the iodine becomes available for general use and when dosage can be so regulated that thyrotoxicosis can be eradicated without danger of producing myxedema The advantage of this method of treatment lies in the fact that the radioactive iodine is administered orally in one or several doses and that the thyroid gland becomes normal in size as thyrotoxicosis is eradicated

THE HEART IN DIABETES

Cardiac manifestations in diabetes may be due to organic changes in the heart, faulty diabetic management or both Organic changes in the heart are usually the result of coronary arterio

sclerosis or hypertension and the more common clinical manifestations are angina pectoris, myocardial infarction and congestive heart failure Faulty diabetic management may be due either to inadequate treatment or overzealous therapy Very important is the fact that the heart in diabetic patients often requires a blood sugar level which is higher than the usually accepted standard for normal persons [271]

Treatment of the cardiac disease itself i e of angina pectoris myocardial infarction or congestive heart failure is discussed under those headings elsewhere Such therapy cannot however, be separated from proper diabetic management directed to the needs of the particular patient since faulty control of the diabetic state may of itself exacerbate the cardiac symptoms

The actual mechanism responsible for production or exacerbation of cardiac symptoms by improper diabetic management is not well understood Severe or abrupt reduction of the blood sugar level either by sharp restriction of carbohydrate intake or by use of insulin which causes a precipitous fall of blood sugar can give rise to symptoms closely resembling those of organic heart disease or may exacerbate the symptoms produced by coexisting angina pectoris, myocardial infarction or cardiac failure [272] Changes in the cardiac status including modifications in the electrocardiogram are known to occur in such circumstances and there are some who believe that absolute or relative hypoglycemia can actually induce angina pectoris and myocardial damage [73] Faulty diabetic management in the opposite direction i e inadequate control of the diabetic state may induce cardiac symptoms or may prevent favorable action of therapeutic measures which are ordinarily beneficial in the foregoing cardiac syndromes It is also possible that dehydration which is not rare in poorly treated diabetes can give rise to tachycardia and other disturbances which may in turn produce cardiac symptoms

Two principles govern the diabetic management of patients with organic heart disease (a) *Acetonuria must be avoided* and (b) *control of the blood sugar level and of the glycosuria must be such as to provide maximum freedom from cardiac symptoms* It is often necessary to permit moderate hyperglycemia and some degree of glycosuria since cardiac symptoms may persist or become aggravated with normal blood sugar levels [7] [73] No rigid rules can be formulated but it is frequently necessary to maintain a fasting blood sugar

level of 150 to 180 mg or permit a loss of 15 to 25 gm of sugar in the urine in twenty four hours in order to obtain relief from cardiac symptoms

DIETETIC MEASURES

The average diabetic with organic heart disease may be given a diet consisting of 60 to 70 gm of protein, 70 gm of fat and 250 gm of carbohydrate The total daily food intake should be arranged so as to provide three moderate meals conforming with mealtimes of the family or to exigencies of the patient's daily routine and in addition to provide a small feeding or snack at midmorning midafternoon and before bedtime Such an arrangement will protect the myocardium against possible absolute or relative hypoglycemia during the waking hours especially if it is necessary to use insulin

Diabetic patients with organic heart disease who are also obese will require a similar feeding arrangement but the total caloric value should be decreased in order that the patient lose weight and thus reduce the load on the heart A reduction in total food intake may be accomplished by decreasing some of the fat and carbohydrate This should be done gradually so that the loss in weight will not exceed 1 pound a week in order to prevent undue weakness and other symptoms

INSULIN

It is generally preferable to use a slower acting insulin such as globin insulin in patients with organic heart disease in order to prevent the wider and more abrupt changes in the blood sugar level which can occur with regular insulin There are no rigid criteria by which one may estimate the correct dosage initially but it will usually be safe to use 1 unit of insulin for every 2 gm of sugar lost in the urine in twenty four hours This amount of globin insulin is injected subcutaneously about thirty minutes before breakfast and the effects are determined by testing pre meal urine specimens for sugar as described on page 86 Determination of dosage is simpler if the patient was well controlled by using regular insulin previously An amount of globin insulin may be then given in the morning equal to about three fourths of the previous total daily dose of regular insulin Here, too the amount of insulin will be regulated by examination of pre meal

urine specimens Increases in globin insulin if necessary may be made by adding 5 units every two or three days while the diet is kept constant until satisfactory control is attained Protamine zinc insulin may be used but the lowest blood sugar level may occur during the sleeping hours at night in contrast to the lowest level with globin insulin which occurs in the late afternoon a time when feeding may be given if deleterious effects are noted Supplementary injections of small doses of regular insulin may be necessary before certain meals if a single dose of slower acting insulin does not control diabetes satisfactorily as shown by pre meal urine specimens

Cardiac symptoms may occasionally persist in spite of careful diabetic management especially if regular insulin is used Relief may sometimes be obtained if about 15 gm of readily absorbable carbohydrate such as lump sugar or fruit juice is taken about two hours after injection of insulin This will tend to offset the tendency to absolute or relative hypoglycemia at the time the insulin exerts its maximum effects [74] The program of 6 feedings daily as outlined previously will also guard against such occurrences and is a schedule well suited for use with longer acting insulin especially in patients with severe heart disease

The treatment of patients in acidosis i e those showing acetone in the urine is the same as described for patients in acidosis shortly after acute myocardial infarction Full details concerning food fluid and insulin will be found on page 86 It is well to remember in this connection that acute myocardial infarction may disturb diabetic control abruptly or may be completely masked by the manifestations of diabetic acidosis or coma

THE HEART IN OBESITY

Symptoms referable to the heart i e dyspnea orthopnea pre cordial pain easy fatigability and swelling of the ankles are en countered frequently in obesity of significant degree Various factors play a part in the production of such symptoms the more important being coexisting hypertension coronary sclerosis and reduced vital capacity due to upward displacement of the diaph ragm It is very likely that the increased burden on the heart occasioned by moving the greater weight of the obese patient is of additional importance There is no unanimity of opinion con cerning the role played by fatty changes in the heart muscle but

it is possible that interference with myocardial efficiency may occur when fatty changes are very marked Regardless of the mechanisms involved, marked relief of the foregoing symptoms is frequently possible by reduction of body weight in obese patients

Treatment of cardiac symptoms apparent or real, in obese patients will consist of measures directed to the heart itself as well as to decrease of the load on the heart by reduction of excessive body weight The therapy of hypertension and manifestations of coronary sclerosis i e, anginal pain or congestive heart failure have been discussed in the chapters dealing with these subjects and need not be repeated Here attention will be directed to reduction of body weight in so far as this applies to obese patients with cardiac symptoms

DIETETIC MEASURES

The most important single element in treatment of obesity is decrease in food intake regardless of the amount which the patient claims he consumes daily Obesity in the great majority of in stances is the result of excessive food intake as compared with the daily expenditure of energy This is generally due to over eating although patients are occasionally seen who store fat on a normal food intake particularly if they have diminished energy expenditure Endocrine disturbances and certain diseases of the central nervous system are frequently held responsible for obesity but such factors are at fault far less frequently than is generally assumed

Reduction of food intake as the sole measure to reduce weight is usually beset with many practical difficulties This is due in part to the fact that the desire for excessive amounts of food is frequently an expression of emotional tension or other psycho neurotic tendencies which are very difficult to control by simple will power Then there are patients who have few normal, active interests in life other than derivation of pleasure from overeating Still others have been induced to overeat during childhood either by example or by parental insistence and have carried this habit into adult life These and other factors which the patient can hardly control, suffice to show that some form of psychotherapy will be necessary in order to maintain the patient s cooperation throughout the entire course of treatment [279] [280] [281] Superficial psychotherapy such as stressing the importance of weight reduc

SAMPLE DIET

Breakfast

1 Choice of

1 Orange	½ Grapefruit with 1 scant tsp sugar
1 Apple	1 Serving fresh strawberries
½ Cantaloupe	

2 Choice of

1 Thin slice of bread (may be toasted)
1/3 Cup all bran
1 Roll (small)

3 1 Egg—boiled or poached

4 1 Glass of skim milk
Tea or coffee as desired

Noon and Evening Meals—for Each Allow

1 Clear stock soup and vegetables

2 Large serving of salad composed of the following

Head of Lettuce	Cabbage
Tomatoes	Beets
String beans	Celery
Carrots	

3 Bread 1 thin slice
or
Potato ½

4 Choice of

Lean beef roast or steak	White chicken
Lean veal	White fish
Lean lamb	2 Eggs

5 Choice of

2 Servings of any of the following

Asparagus	Spinach
Brussel sprouts	String beans
Cabbage	Cauliflower
Sauerkraut	

or

1 Serving of any of the following

Beets	Turnips
Carrots	Squash
Peas	

6 Choice of fruit as for breakfast

Note Do not use FAT in the preparation of food Remove all visible fat from meat Mayonnaise may be made of mineral oil— pint beaten into 1 egg yolk 1 tablespoon vinegar and seasoned with salt pepper mustard and paprika

tion as a general health measure or as a form of treatment which has a directly beneficial effect on the heart may be adequate with some patients It may be necessary, with other patients to attempt an interpretation of their disturbed psychological processes which manifest themselves as a drive to overeat All patients will need constant reassurance and supervision This may be done by having the patient keep a record of his daily food intake as well as of his weight This record should be brought to the physician at weekly intervals so that necessary corrections may be made It will be wise to inform the patient that loss of weight will be rapid during the first few weeks and considerably slower at later periods They should also be told that loss of weight will not be consistent but that it will be interrupted from time to time by periods during which the weight will remain stationary or increase slightly in spite of scrupulous adherence to dietary restriction The foregoing suggestions will prove adequate with many patients but an in determinate number will require deeper psychotherapy by an experienced psychiatrist

Care must be taken in planning a diet for weight reduction that the food is palatable, well balanced and obtainable at restaurants as well as at home A daily intake of 1000 to 1200 calories will generally result in a loss of 1 or 2 pounds a week with little likeli hood of inducing intense hunger, weakness or faintness Unpleasant hunger or weakness, if they do occur can often be prevented by eating small pieces of hard candy containing about 2 to 4 gm of dextrose at intervals of thirty minutes or an hour during the day [277] Such a diet will not prove deleterious to the heart and is more likely to be followed for a long time than one of less caloric value The accompanying sample diet has proved useful although modifications will be necessary from time to time The high roughage content will tend to overcome constipation which fre quently results from a low caloric diet

ACCESSORY MEASURES

Additional measures may be necessary from time to time but these should be used only to tide the patient over difficult periods such as at the beginning of treatment, when the patient becomes discouraged or when the weight becomes stationary

Amphetamine (benzedrine) sulfate can depress the appetite and may be used for this purpose as an aid in weight reduction [278]

Tolerance with loss of effect on the appetite develops in a week or ten days but the effect is restored if the drug is discontinued for about two weeks Hence amphetamine should be used only for short periods and only when indicated, as in the difficult periods mentioned before The usual dosage is 5 or 10 mg thirty minutes before breakfast and lunch An additional 5 mg may be given before supper provided it does not interfere with sleep at night Nervousness restlessness and other untoward symptoms may be allayed by giving phenobarbital, 15 mg (¼ grain) with each dose of amphetamine Hypertension is not a contraindication to the use of amphetamine since such small doses orally hardly affect blood pressure [76, 278]

Thyroid substance in doses of 32 to 130 mg (½ to 2 grains) may be given daily after breakfast to increase combustion of foodstuffs provided the basal metabolic rate is normal or less It too is a temporary expedient to be used in the same manner as amphetamine A notable rise in the basal metabolic rate palpitation nervousness, tremor or increase in pulse rate to 100 per minute require discontinuance of thyroid medication Thyroid substance is not an ideal form of medication in patients with cardiac symptoms since it can also increase the appetite raise the basal metabolic rate or induce tachycardia all of which are undesirable in patients with heart disease

Other measures such as unusual exercise or procedures to induce copious sweating are not necessary and may prove dangerous Prolonged hot baths sweat cabinets and similar measures only increase loss of water and are dangerous Massage while of no particular value may be permitted if it provides a sense of well being

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NEUROCIRCULATORY ASTHENIA

Neurocirculatory asthenia is a clinical syndrome due on the one hand to constitutional inadequacy which is responsible for lack of vigor, undue irritability and easy fatigability and on the other to psychological frustration resulting from inability to adjust to what the patient considers the requirements of his environment. Symptoms of cardiovascular instability are prominent and lead the patient to believe that he is suffering from serious heart disease, a belief which aggravates his symptoms and adds to his discomfort.

Treatment of such patients is thus a difficult and complex undertaking which requires a good psychiatric insight and much tact. The principles in management include reassurance, limitation of aims and activities to bounds within the capacity of the patient and psychiatric therapy to help the patient to adjust himself properly, including finding an outlet for his own capacities in order to minimize the effects of frustration.

It is essential that the physician assume a sympathetic attitude while taking a painstaking history. Any attempt to belittle his complaints or to hurry him may easily give rise to resentment which can ruin any chance of successful treatment.

The examination should be thorough and must include all necessary laboratory tests. It is important to exclude other conditions, such as thyrotoxicosis, incipient tuberculosis or other conditions which may simulate the manifestations of neurocirculatory asthenia.

The patient may then be assured that his symptoms are not due to organic disease, specifically organic heart disease. No ambiguous language may be used and there must be no uncertainty in the attitude of the physician when the integrity of the patient's heart is discussed. It is very necessary to explain to the patient that his symptoms, although real to him, are due to his attempts to accomplish more than his capacities permit or that

he is laboring under strain of emotional difficulties which are the real cause of his discomfort A common mechanism is identification of the patient with some one who died of heart trouble Other precipitating factors are the accidental discovery of a functional murmur or a tactless remark by a physician which leads the patient to believe that his heart is not in good condition Still other possibilities are domestic worries, jealousies, economic difficulties, or guilt feelings of various sorts All of these require frank discussion with advice as to the best way to avoid or reduce such difficulties

Re education is the next step The patient should be guided in selecting an occupation which will not tax his physical and nervous capacity Social activities, exercise and other activities should not be pushed to the limits of the patient s endurance Great tact will be necessary in the attempt to confine activities to bounds within the patient's capacity without at the same time making the patient conscious of his constitutional inadequacy It should be stressed that we are not all suited for the same kind of work and that some of the world s best work has been accomplished by persons of his constitutional make up

Drugs play a minor role in the treatment of neurocirculatory asthenia Under no circumstances should digitalis or other ' cardiac remedies be employed as this will awaken the suspicion that heart disease is actually present Mild sedatives may be employed for nervous tension or to induce sleep but these should be discontinued as soon as possible Many patients will respond favorable to the foregoing measures but the physician should not hesitate to recommend the aid of a well trained psychiatrist if satisfactory progress has not been made

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THE HEART IN VITAMIN DEFICIENCY

THE HEART IN BERIBERI

Symptoms resembling cardiac failure are encountered in beriberi but these will not be benefited appreciably by digitalis mercurial diuretics or other measures employed in congestive heart failure The underlying cause is deficiency in thiamine and only administration of thiamine will result in striking improvement

Thiamine is best administered parenterally in such instances since absorption from the gastro intestinal tract is uncertain Treatment may be commenced with intravenous injection of 25 mg of thiamine hydrochloride three times daily Multiple injections daily are desirable since excretion is rather rapid The same dosage may then be given by intramuscular or subcutaneous injection after a favorable response becomes apparent Striking improvement with copious diuresis temporary bradycardia and transient elevation of blood pressure are noted within a few days [82] Reduction in size of the heart and return of electrocardiographic abnormalities to normal may be expected somewhat later There need be no fear of toxic effects from such doses of thiamine

Additional measures such as bed rest and a well balanced high caloric diet are of value Other nutritional deficiencies such as pellagra or scurvy frequently coexist and require treatment with appropriate remedies Organic heart disease due to factors other than thiamine deficiency may be present It will be wise in such instances to use thiamine until maximum benefit is attained before employing other cardiac management It will thus be possible to evaluate the degree to which thiamine deficiency is responsible for production of the cardiac symptoms Residual evidences of cardiac impairment may then be treated as outlined under management of the various syndromes

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HEART DISEASE IN PREGNANCY

Pregnancy imposes a gradually increasing burden on the heart slowly at first, but more rapidly after the beginning of the fifth month to reach a maximum increase of about 50 per cent at the end of the eighth month The load on the heart becomes reduced during the last three or four weeks of pregnancy to again sustain a temporary increase during labor It is important to remember that delivery whether at term or before normal or induced and whether vaginal or in the form of abdominal hysterotomy all constitute an additional burden of considerable magnitude[283, 284] It would seem that delivery at any time would result in immediate relief of congestive heart failure but experience has shown that this is not true In fact it has been observed that heart failure may become worse immediately *after* delivery[83]

The strain of pregnancy and labor is almost never too great for the healthy heart Patients with organic heart disease who have little or no cardiac enlargement and who have no previous history of congestive failure or auricular fibrillation will generally experience little difficulty during pregnancy Such patients may be treated in the same manner as those with healthy hearts but they should be observed at intervals of two or three weeks and at shorter periods after the beginning of the fifth month of pregnancy More frequent examination for evidences of cardiac embarrassment in the last half of pregnancy is advisable because of the increasing load on the heart and because cardiac failure may arise rather abruptly and without much warning

The strain of normal labor will seldom induce cardiac failure if no heart failure occurred in the past or during pregnancy This is especially true if the second stage of labor is shortened or eliminated by episiotomy and application of low forceps as soon as the os is fully dilated It must not be forgotten, however that labor or delivery by any route can aggravate heart failure seriously *if already present* during pregnancy or at the time of delivery

Patients who have a history of cardiac failure or auricular fibrillation or who develop these during pregnancy will require very close supervision It is best that pregnancy be avoided in such patients as well as in those who have an additional but unrelated serious illness The same is true of patients with rheumatic or congenital heart disease who are more than thirty five years of age unless the heart is in a very good functional state [283-87] Pregnancy should also be avoided if the patient has had reactivated rheumatic fever or carditis shortly before contemplated pregnancy Subacute bacterial endocarditis need no longer be considered a contraindication to pregnancy or to continuation of the pregnancy

PREVENTION OF CARDIAC FAILURE DURING PREGNANCY

It is of the utmost importance to prevent cardiac failure in pregnant patients with organic heart disease Such patients should spend nine or ten hours in bed every night and should rest on a couch or in bed for at least an hour after lunch during the first four months The rest period during the day should be lengthened in the last half of pregnancy and for several weeks after delivery Stair climbing, house work shopping tours and social activities should be reduced to a minimum Acute infections may be a factor in precipitation of cardiac failure hence, the patient should avoid exposure in inclement weather Attendence at public gatherings or other places where contact with infectious diseases is possible should be curtailed Isolation from friends or members of the family who harbor acute infections is advisable

Obese patients should live on a low calorie diet in order to reduce weight Anemia should be treated by iron if of the hypochromic type and by intensive liver therapy if of the macrocytic variety Thyrotoxicosis if contributing to cardiac embarrassment should be treated surgically if necessary Propylthiouracil is apparently a much safer drug than thiouracil if it is desirable to avoid surgery during pregnancy Propylthiouracil may be given in doses of 50 mg three or four times daily Complete blood counts should be made at intervals of a week although serious effects on the blood have been very rare so far In short, all precautions should be taken to improve the general condition of the patient as much as possible

TREATMENT OF CARDIAC FAILURE DURING PREGNANCY

The patient should be instructed to report immediately such symptoms as dyspnea or cough for which there is no apparent cause or an increase of dyspnea following a degree of exertion which did not cause such shortness of breath previously Other warning symptoms are epigastric discomfort nocturnal dyspnea or asthma, orthopnea or hemoptysis The presence of *persistent* rales at the bases of the lungs, increase in congestion of the veins in the neck or tenderness of the liver are reliable objective signs of cardiac failure They are definite indications to place the patient at bed rest and to institute treatment for congestive heart failure

The actual treatment of congestive heart failure during pregnancy differs very little from the methods employed in nonpregnant patients as described on page 53 Morphine and its allies should be used sparingly shortly before or during delivery in order to avoid the depressant effects on the fetus Demerol 50 to 75 mg intramuscularly, has been found effective and harmless and may be repeated at intervals of three or four hours Pleural effusion if great enough to contribute to persistence of dyspnea should be removed at once by aspiration

Patients who develop cardiac failure at any time during pregnancy should be kept in bed preferably in a hospital until after delivery [286] In no event should the patient be permitted to leave her bed until three weeks have elapsed after all signs of cardiac failure have disappeared

MANAGEMENT OF PREGNANCY IN PATIENTS WITH HEART DISEASE

It is justifiable to interrupt pregnancy by vaginal curettage during the first two months in patients who have a history of cardiac failure or auricular fibrillation or flutter in the past Failure to interrupt pregnancy in such patients at this time may permit the load on the heart to increase to a dangerous degree in the latter half of pregnancy with serious results [285] Interruption of pregnancy during the first two months is mandatory if cardiac failure or auricular fibrillation develops during this stage It is essential that the cardiac failure be improved as rapidly

as possible and that the heart rate in auricular fibrillation be *slowed to nearly normal by appropriate treatment before interruption of pregnancy* is undertaken. It is almost certain that the burden of pregnancy will ultimately increase beyond the capacity of the patient with further progress of pregnancy in such patients. Early interruption of pregnancy is also indicated if rheumatic fever or rheumatic carditis become activated shortly before or during early pregnancy. The development of subacute bacterial endocarditis during pregnancy need cause no alarm since adequate treatment with penicillin may permit successful delivery at term provided no other complications develop.

Patients who develop cardiac failure after the second or third month of pregnancy but before the fifth month face the certainty that the load on the heart will increase rapidly with the beginning of the fifth month. Such patients should be hospitalized at once and energetic treatment should be instituted for the cardiac failure. Pregnancy should be interrupted by abdominal hysterotomy as soon as maximum improvement of cardiac failure is attained. *Sterilization should be advised since cardiac failure is likely to recur during subsequent pregnancies.*

Patients who develop cardiac failure for the first time after the beginning of the fifth month of pregnancy or where failure developed before but could not be improved by therapy should be treated conservatively. It would seem that interruption of pregnancy *in such patients would relieve the load on the heart.* Experience shows that the contrary is the case. Delivery by any method during cardiac failure increases the load on the heart, which is already too great and is thus very dangerous. The puerperium is a further danger point since cardiac embarrassment may be increased further by significant reduction in vital capacity as *well as by other factors. Patients who develop cardiac failure* after the beginning of the fifth month of pregnancy should be treated intensively for congestive heart failure as outlined on page 53 with the hope that the reduction of the load on the heart which occurs automatically during the last three or four weeks of pregnancy will prove sufficient to permit successful delivery.[283-287] *Here too,* pelvic delivery is preferable since abdominal hysterotomy has been shown to be attended by a higher maternal death rate.[284]

Barbiturates and scopolamine are used frequently before and during labor and delivery for sedative effects They may make the patient very restless and may cause her to toss about violently with disastrous effects on the diseased heart It is better to use demerol in doses of 50 to 100 mg intramuscularly with repetition at intervals of two or more hours to relieve pain and to quiet the patient during labor and delivery Adequate sedation may be attained with demerol and no ill effects have been noted in the fetus Demerol may be given as soon as the patient begins to complain or when the os is dilated to about 5 to 7 cm

Pituitrin may prove undesirable in patients with organic heart disease Ergonovine has been used in such instances with success and without deleterious effects on the heart

The form of anesthesia to be used at the time of delivery in patients with organic heart disease is of great importance *Delivery at term in patients with fully compensated hearts* presents no difficulties Ether anesthesia is probably the safest inhalation anesthetic for *pelvic delivery at term* Parasacral or pudendal anesthesia may also be used in such patients as may almost any other anesthetic if administered by a skilled anesthetist *Abdominal hysterotomy at term in patients with fully compensated hearts* may be performed under ether anesthesia or local infiltration (field block) Continuous low spinal anesthesia may be used in such patients by those skilled with this procedure provided close watch is kept on the blood pressure Abrupt fall in blood pressure responds quickly to immediate intravenous injection of 5 mg of desoxyephedrine hydrochloride followed at once by an intramuscular injection of 10 to 15 mg as a sustaining depot The intravenous injection of 5 mg may be repeated at intervals of five minutes until systolic blood pressure rises well above 100 mm Hg or a maximum of 15 mg have been given intravenously Desoxyephredrine produces no deleterious effects on the heart in fact the author has used desoxyephedrine successfully in similar dosage in shock following acute myocardial infarction Any of the foregoing methods of anesthesia may of course be used in interruption of pregnancy before term in such patients

Cardiac failure shortly before or during labor or delivery is a serious matter when it occurs at term or before *Pelvic delivery* may be attempted under pudendal block or under ether by inhalation if

block anaesthesia is unsatisfactory *Abdominal hysterotomy* in the presence of cardiac failure may be performed under local infiltration as the method of choice Ether anesthesia by inhalation may be necessary where local infiltration is impracticable *Pelvic delivery by manipulation* will be best accomplished with the aid of ether

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SURGERY AND HEART DISEASE

It is often necessary to appraise the risk of surgical operation in patients with organic heart disease. Several factors must be considered before a decision can be made, the more important being the type of cardiac involvement, the presence or absence of congestive heart failure and the probable extent and duration of the operation. Hardly less important is a consideration of the actual need for operation, i.e., whether surgery is urgently necessary to save life, whether it is indicated to improve health or whether it is designed merely to increase the patient's comfort.

THE PROBABLE RISK OF OPERATION IN VARIOUS FORMS OF HEART DISEASE AND HYPERTENSION

VALVULAR HEART DISEASE

Little or no additional risk is entailed if valvular heart disease is not associated with a history or evidence of congestive heart failure, if the heart is not greatly enlarged, if there is no heart block or if the ventricular rate is not rapid. Exception must be made in high grade aortic valve stenosis or incompetency and in cardio-aortic syphilis where sudden death is possible. In general it may be stated that no difficulties need be expected in patients with valvular disease or in almost any form of heart disease if the patient was able to keep up his ordinary activities without significant distress. It will be well in this connection to re-emphasize that surgical or dental manipulation of an infected focus may precipitate subacute bacterial endocarditis in patients with valvular or congenital heart disease. Such patients should receive prophylactic therapy with penicillin as outlined in the chapter on treatment of subacute bacterial endocarditis.

CONGESTIVE HEART FAILURE

The presence of congestive heart failure or a history of its occurrence in the past constitutes a serious risk and no operation

should be performed in such patients unless urgently necessary to save life Congestive heart failure can be recognized by a careful history and a meticulous physical examination rather than by instrumental or laboratory aid Particular attention should be paid to dyspnea on ordinary exertion unless it can be explained on some other basis Nocturnal dyspnea, wheezing at night, orthopnea hemoptysis or nocturnal cough are very suggestive of pulmonary congestion in patients with heart disease, even if rales or other physical signs of pulmonary engorgement are absent It is precisely in such patients that transfusions and intra venous fluids are dangerous Congestive heart failure may also be recognized by the presence of persistent rales at the bases of the lungs by Cheyne Stokes respirations edema of the feet and cyanosis or punch tenderness of the liver Roentgenographic examination of the chest may disclose a very large heart or sig nificant congestion of the pulmonary artery tree but these findings will seldom come as a surprise if a careful history is taken and a complete physical examination is made

CORONARY HEART DISEASE

Coronary heart disease may manifest itself is congestive heart failure angina pectoris or myocardial infarction The risk of operation is considerable in the group as a whole since such pa tients are in an older age group with diminished recuperative powers and with frequent coexisting degenerative changes in other regions of the body These considerations and the fact that patients with coronary heart disease have a limited life expectancy in general warrant conservatism in recommending surgery It may be stated that surgery may be contemplated only in the case of urgent operations to save life or surgery which is imperative for reasons of health

Coronary heart disease with congestive failure constitutes a very serious risk The manifestations of cardiac failure are similar to those described under valvular disease of the heart and the same care should be exercised in eliciting a careful history and in performing a complete physical examination The risk is greater when congestive heart failure is due to coronary disease for the reasons enumerated in the preceding paragraph

Coronary heart disease with angina pectoris constitutes a very grave risk unless the anginal attacks are mild and infrequent

Patients with more frequent or more severe attacks may die suddenly at any time It may prove useful to administer about 1/3 mg (1/150 grain) of nitroglycerine under the tongue just before anesthesia and to repeat this every thirty minutes during the operation in order to prevent anginal seizures The situation is complicated further by the liability of patients with coronary heart disease to develop myocardial infarction postoperatively This may occur within the first few days without pain or the clinical picture may be masked by sedatives or narcotics Post operative shock abrupt dyspnea or cyanosis may be the chief manifestations in such patients hence the occurrence of such symptoms should awaken strong suspicion that myocardial in farction has occurred [88]

Myocardial infarction is a very serious risk and no surgery should be attempted during its early stages unless imperative to save life It is better to defer surgery if possible for at least three months after the attack in order to allow adequate time for good healing of the infarcted area

CARDIOAORTIC SYPHILIS

Patients with moderate uncomplicated syphilitic aortitis gener ally withstand operation well The risk is very great in the pres ence of congestive heart failure aneurysm significant involve ment of the aortic valve or in narrowing of the coronary ostia

Congestive heart failure in cardioaortic syphilis is a very serious matter Such failure is often very resistant to treatment and the average duration of life is generally very limited Only life saving operations are permissible in such patients Elective operations may be planned only if the congestive failure responds well to treatment and if the contemplated operation is very necessary from the standpoint of the patient s health

Aortic valve involvement when of moderate degree as judged by the patient s ability to perform his ordinary work without difficulty may be regarded as a moderate risk The risk is not great enough however to preclude surgery which is necessary to save life or to improve health The risk is much greater and sudden death is possible if the aortic valve involvement is sufficiently advanced to cause anginal pain or manifestations of cardiac failure Aneurysms which cause symptoms are dangerous for the same reasons

Narrowing of the coronary ostia may be suspected if anginal pain is experienced but it is not possible to gauge the degree of narrowing by the severity of the pain It is a dangerous complication in any event and none but very urgent surgery may be performed in such patients when the condition is suspected

HYPERTENSION AND HYPERTENSIVE HEART DISEASE

Uncomplicated hypertension even if the systolic pressure is above 200 mm Hg, adds little to the risk of operation Cardiac or cerebral complications increase the risk materially while renal involvement or malignant nephrosclerosis practically preclude any but the most urgent of life saving operations Equally serious are a history or presence of congestive heart failure or angina pectoris The life span in such patients is relatively short and all dangers incident to such conditions as described under coronary heart disease are applicable in these patients Renal complications are particularly serious because uremia may be precipitated Active nephritis, blood urea of more than 35 mg per 100 cc of blood or the presence of considerable albumin in the urine, or significant numbers of casts or red blood cells must be considered as evidences of greatly increased operative risk

Cerebral complications which are transient or of brief duration need not interfere with emergency operations However it is better to wait for three or four weeks if such a delay is possible Necessary operations may be performed in more significant cerebral accidents when a period of about three months has elapsed without evidence of further progression Other factors such as the age of the patient, the degree of his incapacity, the probable life span and the actual need for the operation must also be taken into consideration before deciding on surgical interference

ACTIVE INFLAMMATORY DISEASE OF THE HEART INCLUDING RHEUMATIC CARDITIS SUBACUTE BACTERIAL ENDOCARDITIS AND DIPHTHERITIC MYOCARDITIS

It will be wise to defer operation in active rheumatic involvement of the heart until all signs of activity have been absent for a period of at least six months No patient with active rheumatic heart disease should be subjected to operation unless it is very urgent since the smouldering process in the heart may flare up and give rise to serious consequences

Our conceptions regarding the danger of surgical operation in patients with subacute bacterial endocarditis have been altered radically since the introduction of penicillin in the treatment of this condition It is now possible to attain permanent arrest of the infection in about 75 per cent of all cases Sufficient time has elapsed to warrant the statement that recurrence is very rare once the infection is arrested by adequate treatment with penicillin It seems that unlike rheumatic heart disease there is little possibility of reactivating a smouldering focus of activity within the heart by surgical operation We have submitted patients to such major surgical procedures as Cesarean section without mishap after signs of active infection had been absent for three weeks Surgical procedures should of course be regulated in accordance with the degree of permanent residual cardiac damage and the presence or absence of congestive heart failure as outlined under valvular disease

Diphtheritic myocarditis is a serious condition in which sudden death is possible Hence it will be wise to wait for at least six months or a year alter all signs of active involvement have subsided before submitting such patients to operation It is fortunate that no permanent damage to the heart is incurred by diphtheria No additional risk will thus be encountered if operation can be deferred as outlined until all active involvement in the myocardium has subsided

THYROTOXICOSIS AND HEART DISEASE

This subject has been dealt with in Chapter 10 Here it may be reiterated that surgical eradication of thyrotoxicosis is still the most dependable method of removing the additional burden imposed by disturbed thyroid function Hemithyroidectomy may be performed if cardiac disability is very severe with removal of the remaining thyroid tissue after noticeable improvement has taken place It is noteworthy that thyrotoxic patients with cardiac involvement withstand operation surprisingly well if properly prepared for surgery

CONGENITAL HEART DISEASE

The successful treatment of congenital heart disease by surgery has demonstrated that patients with such lesions can withstand long and difficult operations well The presence of cyanosis seems

Narrowing of the coronary ostia may be suspected if anginal pain is experienced but it is not possible to gauge the degree of narrowing by the severity of the pain It is a dangerous complication in any event and none but very urgent surgery may be performed in such patients when the condition is suspected

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broken In general it may be said that the condition of the myocardium rather than the arrhythmia is of prime importance

ANESTHESIA

THE CHOICE OF ANESTHESIA

The choice of an anesthetic for patients with organic heart disease will depend on several factors The anesthesia must be safe, it must induce anesthesia quickly in order to minimize preoperative excitement and struggling it must furnish an adequate concentration of oxygen in order to prevent anoxia and it must provide satisfactory working conditions for the surgeon Equally important are the skill of the anesthetist and his familiarity with the anesthetic which is to be used

PREOPERATIVE MEDICATION

Preoperative medication is very important since it allays apprehension and excitement induction of anesthesia is smoother and less anesthetic will be required General anesthesia should be preceded by a subcutaneous injection of morphine or morphine with scopolamine or atropine in the proportion of 1 25 Demerol 100 mg, may be injected instead of morphine in order to avoid nausea and vomiting This premedication may be given about one and one half hours before the anesthetic is started Regional and spinal anesthesia require heavier preliminary sedation in order to decrease reactions from traction and other operative manipulations A short acting barbiturate such as seconal or nembutal in doses of 0 1 to 0 2 gm may be given two hours before the anesthetic is started, in addition to the measures outlined for general anesthesia

GENERAL ANESTHESIA

Inhalational anesthesia by the closed method is the procedure of choice Induction of anesthesia is smooth it permits adequate concentrations of oxygen so important in heart disease and the depth of anesthesia can be controlled almost at will Rapid induction of anesthesia can be attained by beginning with ethylene or cyclopropane preferably the former because it has much less tendency to induce cardiac arrhythmia than cyclopropane This need not be a serious indictment against cyclopropane since pre

to offer little difficulty even if associated with multiple cardiac defects. It has been stated that there may be some danger when there is a shunt of blood from the left to the right side of the heart if struggling incident to anesthesia or the strain of operation reverses the direction of flow. There is as yet insufficient data from which to draw far reaching conclusions but it would seem that patients with congenital heart disease should withstand operations elsewhere in the body as well as operations upon the heart itself. Nevertheless, it will be wise in the meantime to limit surgical procedures in such patients to operations of real necessity until more information becomes available.

HEART BLOCK AND CARDIAC ARRHYTHMIA

Any form of heart block is a definite risk for patients requiring an operation. The risk is greater in heart block with dropped beats than in the simpler forms. Intraventricular or bundle branch block is generally due to wide spread myocardial disease and should be regarded as a serious risk. The risk is very great and sudden death is possible in Adams Stokes syndrome. Only very urgent surgery is permissible in heart block unless the block is of the simplest form. Auricular fibrillation or flutter which is not associated with serious myocardial disease or with evidence of congestive heart failure does not add materially to the risk of operation. Attempts should be made before operation to slow the heart rate within the normal range with digitalis whenever possible. Premature beats (extrasystoles) are of little or no significance unless associated with serious heart disease in which case it is the cardiac condition rather than the arrhythmia which will determine the degree of risk. It will be wise, however, to avoid cyclopropane in such patients in order not to aggravate the arrhythmia by the anesthetic agent. Paroxysmal tachycardia of short duration is no contraindication to operation, nor should the operation be interrupted if such tachycardias develop during surgery. The normal heart will not be injured unless the paroxysm lasts many hours and even a diseased heart will tolerate such tachycardias for a few hours. Carotid sinus pressure and other measures described in Chapter 4 may be employed although the attacks usually cease spontaneously after operation. Ventricular tachycardia is a very serious risk to operation and no surgery should be attempted if it can possibly be avoided until the paroxysm is

This form of anesthesia is safe, well tolerated and is practically free from undesirable reactions The usefulness of ordinary spinal anesthesia is limited in patients with heart disease because of the possibility of a rapid fall in blood pressure which may induce serious consequences in such patients The measures employed to combat or prevent such a drop in blood pressure namely ephedrine and its allies are in themselves not harmless since they may induce anginal attacks or give rise to various arrhythmias in susceptible patients

THE MANAGEMENT OF CONGESTIVE HEART FAILURE AND OTHER CARDIAC DISTURBANCES BEFORE OPERATION

EMERGENCY OPERATIONS

Patients in congestive heart failure may require an emergency operation to save life or for some other imperative reason Such patients may be given an immediate slow intravenous injection of 0 5 mg of strophanthin K if no digitalis was used in the preceding four or five days A smaller amount 0 25 mg may be administered if congestive heart failure is present in spite of the previous use of digitalis Any injectable preparation of digitalis may be used intravenously in amounts equal to the potency of 0 5 gm of the powdered leaf if such a preparation is preferred to strophanthin Strophanthin acts more rapidly than most preparations of either digitalis purpurea or lanata and has the further advantage that the ordinary daily requirement is used up completely or eliminated in twenty four hours i e cumulative symptoms are less likely An adequate amount of strophanthin or digitalis if given when the patient is first seen can result in significant improvement of congestive heart failure by the time the patient is prepared for emergency operation An additional 0 25 mg of strophanthin or one half of the initial dose of injectable digitalis may be given intravenously after the patient is returned from the operating room if the first dose has produced no significant improvement of the cardiac status Similar amounts of strophanthin or injectable digitalis may be continued once daily for maintenance effect until digitalis can be given orally

Intravenous administration of blood plasma or other fluids are frequently necessary in emergency surgery These should be given

mature beats, when caused by inhalational anesthesia may often be abolished by an adequate supply of oxygen Anesthesia may be maintained after induction by addition of ether to the anesthetic mixture and by varying the concentration of the other gases The foregoing method may be used in patients with almost any form of heart disease who require a general anesthetic for abdominal or pelvic surgery or other type of operation The same method may be used in emergency surgery if congestive heart failure is present when field block or a combination of field block and light ethylene ether anesthesia is not practicable Nitrous oxide is best avoided in angina pectoris or congestive heart failure because of its possible ill effects from anoxia

LOCAL ANESTHESIA

Local anesthesia with a 1 or 2 per cent procaine solution which does not contain epinephrine may be used safely in patients with heart disease Epinephrine and its allies should be omitted because of the tendency to induce anginal attacks in patients with coronary sclerosis and palpitation or arrhythmia in other forms of heart disease Procaine exerts no deleterious effects on the heart unless significant amounts are injected intravenously by accident Unpleasant side reactions may be prevented by oral administration of about 0 1 gm ($1\frac{1}{2}$ grains) of a short acting barbiturate about an hour before the local anesthetic is injected Additional preliminary sedation with morphine or morphine and scopolamine may be useful in very apprehensive patients

FIELD BLOCK AND REGIONAL NERVE BLOCK ANESTHESIA

The principles described for local anaesthesia are applicable in field block and regional nerve block anesthesia Experience has shown that amounts of procaine up to 1 gm i e 50 cc of a 2 per cent or 100 cc of a 1 per cent solution may be used without danger of untoward reaction Field block is a useful method in many types of operation, including thyroidectomy Supplementary, light gas anesthesia may be necessary in some instances or where the patient is very apprehensive

CAUDAL LOW SPINAL AND SPINAL ANESTHESIA

Low spinal anesthesia or caudal block, with minimal dosage, is the anesthetic of choice for prostatic, rectal or perineal operations

This form of anesthesia is safe well tolerated and is practically free from undesirable reactions The usefulness of ordinary spinal anesthesia is limited in patients with heart disease because of the possibility of a rapid fall in blood pressure which may induce serious consequences in such patients The measures employed to combat or prevent such a drop in blood pressure namely ephedrine and its allies are in themselves not harmless since they may induce anginal attacks or give rise to various arrhythmias in susceptible patients

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Intravenous administration of blood plasma or other fluids are frequently necessary in emergency surgery These should be given

with great caution and in accordance with the principles laid down in the section dealing with parenteral fluids in patients with heart disease It is difficult to estimate the capacity of the cardiovascular system for parenteral fluids when congestive heart failure is present There may be only minimal signs of pulmonary congestion but there are no positive criteria by which to recognize such dangerous conditions as a narrow fish mouth mitral stenosis This is illustrated by a twenty six year old patient who was admitted during her fourth month of pregnancy with a history of exertional dyspnea some hemoptysis and wheezing respirations at night She had clinical signs of aortic incompetency and mitral valve involvement but there were no rales or other signs of pulmonary engorgement Abdominal hysterotomy for interruption of pregnancy was recommended because her heart failed to improve after bed rest and digitalis A blood transfusion of 500 cc was given slowly over a period of three hours the day before operation because of well marked anemia Thoracic oppression, wheezing breathing and marked dyspnea developed just as the transfusion was finished All treatment was of no avail and the patient died a few hours later Autopsy revealed rheumatic aortic valve incompetency and a markedly narrowed mitral orifice which barely admitted one finger The lungs were firm and brownish and showed evidences of marked congestion It was felt that the addition of 500 cc of blood was more than her heart could pump through the very narrow mitral orifice and that the resulting severe pulmonary congestion was the chief cause of death

Transfusion of blood may however be necessary as an emergency measure in hemorrhage or very severe anemia in spite of coexisting heart disease Transfusions which furnish about 50 cc at intervals of an hour may be of help without overloading the circulation Larger amounts of blood or plasma given at a faster rate may be imperative in shock It will then be necessary to weigh the urgent needs of the patient against the probable capacity of his heart to handle the additional fluid and to take such calculated risks as the occasion may demand Other fluids if very necessary may be given slowly by continuous intramuscular infusion in order to decrease the possibility of abrupt overloading of the circulation The method is essentially the same as for hypodermoclysis except that the needle is inserted and fixed deeply into the muscle mass on the outer aspect of the thigh Not more than

1000 cc of physiologic solution of sodium chloride should be administered in twenty four hours but a similar amount of 5 per cent dextrose in water is safer

Patients with angina pectoris should not be submitted to surgery unless operation is imperative Adequate sedation with morphine or other sedatives should be employed before operation Nitroglycerin, 1/3 mg (1/150 grain), may be placed under the tongue before operation and at subsequent intervals of thirty minutes until the patient is returned to his bed The same precautions should be used in regard to intravenous fluids as were outlined under congestive heart failure The physician should be on the alert for the occurrence of myocardial infarction after operation Pain may be absent or masked by narcotics but postoperative shock dyspnea or cyanosis may be the only manifestation of coronary thrombosis in patients with coronary artery disease

PARENTERAL FLUIDS AS A RISK IN PATIENTS WITH HEART DISEASE

The need for a normal water and electrolyte balance before and after operation may lead to an injudicious use of parenteral fluids in patients with heart disease The tolerance of patients with heart disease for salt and fluids is much less than in persons with normal hearts It has been shown that addition of 10 gm of salt to the regular salt intake of a patient can induce cardiac failure in patients recently recovered from congestive heart failure On the other hand oral ingestion of as much as 3000 cc of water caused no such difficulties provided the salt intake was not increased [89] It is well to remember in this connection that both blood and plasma have an appreciable sodium content hence they should be used with caution in patients with heart disease

Recent studies have shown that both the blood and plasma volumes increase almost in direct proportion to the speed of intravenous injection of isotonic solutions for the first thirty minutes after which the blood volume tends to return to normal levels With inflow of 2000 cc or more the circulating blood volume does not tend to return to its initial level but continues to increase although at a diminishing rate [290] Hence it is important to regulate the speed as well as to restrict the amount of intravenous fluids in patients with organic heart disease

Patients with heart disease, especially those with a history or evidence of congestive heart failure or angina pectoris, should be given fluids with caution Intramuscular injection of 1000 cc of 5 per cent dextrose in water (not saline solution) daily will be safe Intravenous administration, if necessary, may consist of 500 cc of 5 or 10 per cent dextrose in water at any one time The rate of flow should be slow, not more than 10 to 15 cc per minute Physiologic solution of sodium chloride should not be used in patients who have recently recovered from congestive heart failure or who are in failure particularly if they have the slightest evidence of pulmonary congestion The same is true of patients with angina pectoris Oral administration of fluids in amounts up to 2000 cc daily are safest and should be started as soon as possible Blood transfusions because of the sodium content, should be given very slowly and should be discontinued immediately on the first complaint of cough tightness in the chest wheezing respirations or dyspnea It is best in any event to give not more than 250 cc of blood at one time and twice in one day if necessary

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